EXCIPIENT COMPOSITIONS FOR TABLETTING AND PROCESSES OF PREPARATION THEREOF.

The present invention relates to excipient composition for tabletting comprising diluents, binders, anti adherents, lubricants and disintegrants. The excipient composition of the present invention comprises all ingredients except the active pharmaceutical ingredient (API). The present excipient compositions find utility in formulating tablets by direct compression; dispersible tablet, sustained release tablets, and composition blend for moisture sensitive or hygroscopic active pharmaceutical ingredients. The excipient composition of the present invention offers significant economic advantage over the conventional techniques.

We Claim:

1. An excipient composition for tabletting comprising:
    a. 65 to 90 % w/w diluent;
    b. 0 to 1.0 % preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. 0 to 20% w/v disintegrant
    e. 0.5 to 15 % w/w lubricant
    f. 0 to qs organoleptic additives.

2. The excipient composition for tabletting as claimed in claim 1 for dispersible tablet comprising:
    a. 65 to 85 % w/w diluent;
    b. 0 to 1.0 % w/w preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. 5 to 20 % w/w disintegrant; and
    e. 2 to 10 % w/w lubricant.
    f. 0 to qs organoleptic additives.

3. An excipient composition for tabletting as claimed in claim 1 for direct compression of moisture sensitive or hygroscopic active pharmaceutical ingredients comprising:
    a. 70 to 85 % w/w diluent;
    b. 0 to 1.0 % preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. optionally a disintegrant q.s. % w/w
    e. 2 to 15 % w/w lubricant
    f. optionally, organoleptic additive q.s. % w/w

4. A tabletting process for preparation of excipient composition comprising steps:
   i. mixing diluents, binder, anti-adherents for 20 minutes in rapid mixer granulator;
   ii. preparation of a binder paste solution in stem jacketed paste making kettle and cooling the resultant paste to 40 to 45 degree Celsius;
   iii. granulation of step i mixture along with the binder paste of step ii;
   iv. wet milling the granules of step iii;
   v. drying the granules of step iv;
   vi. sifting the dried granules through 20# mesh using vibrator sifter;
   vii. milling the sieved granules through multi-mill;
   viii. adding lubricant sifted through 40# to granules of step vii, in an octagonal blender.

5. The excipient composition for tabletting as claimed in any of the preceding claims wherein the diluent is selected from MCC, HPMC, ethyl cellulose, lactose, starch, di-calcium phosphate or mixtures thereof.

6. The excipient composition for tabletting as claimed in any of the preceding claims wherein the binders or adhesive is selected from pre-gelatinized starch, Starch, polyvinyl pyrrolidine of different grades, gelatin, gums or mixtures thereof.

7. The excipient composition for tabletting as claimed in any of the preceding claims wherein one or more disintegrants are selected from sodium starch glycolate (SSG), croscarmellose sodium, crospovidone, fumed silicon dioxide, starch or mixtures thereof.

8. The excipient composition for tabletting as claimed in any of the preceding claims wherein lubricant is selected from talc, magnesium stearate, fumed silica, colloidal silicon dioxide or mixtures thereof.

9. The excipient composition for tabletting as claimed in any of the preceding claims wherein organoleptic additive may be colorant, flavoring agent or sweetener.

Dated this the 14th day of June 2013

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FIELD OF INVENTION

The present invention relates to excipient compositions for tabletting. The present invention more particularly relates to excipient composition for tabletting comprising diluents, binders, anti-adherents, lubricants, disintegrants and optionally organoleptic additives.

BACKGROUND OF THE INVENTION

In pharmaceutical formulations, excipients of various categories such as diluents, binders, lubricant/anti adherents, and/or disintegrants exclusively used as single ingredient that play a particular role. The convention formulating processes involve conventional manufacturing methods like direct compression, wet granulation, dry granulation wherein desired excipients are added to API or vice versa. Conventional oral tablets for ingestion in addition to the active ingredient contain same class of components wherein one or more agents are functioning as 1) a diluent, 2) a binder or an adhesive, 3) disintegrating agent and 4) a lubricant. All non-drug components of a formula are termed as 'excipient (s).'

During preparation of final oral dosage form, especially tablets, the most commonly employed means is to blend the API with the appropriately formulated excipients followed by compression of the resultant mixture. This formulation with the excipient is not a single step but a series of sequential additions and processing wherein a particular category of the ingredients are added at particular stage and mixed or granulated as the case may be. Conventionally, material is typically blended with the API and compressed. The materials include diluents or filler/carriers, binders or adhesives, disintegrant, glidants/lubricant, colorants, flavorants or mixtures thereof.

Glidants and/or lubricants are added just before compression as addition of these agents with the other excipients could result in tablet with unacceptable hardness. This may further affect tablet disintegrating properties negatively.

Ready-to-use co-processed excipients consisting of diluent-binder-disintegrating agent are known. Here the API, the co-processed excipients comprising lubricants are mixed together. These are combined excipients which consist of numerous individual substances such as filler, binding agent and disintegrating agents; which are produced by wet granulation. These multi-functional substances demonstrate certain advantages over the physical mixture of the individual components on flowability, hardness, friability, etc.

Direct compression comprises steps of mixing the active ingredient with the excipient and then punched into tablets.

Combinations of filler, binder and disintegrating agents known as co-processed excipients are known. Several patents have reported various compositions and the process for making these excipient blends but none yield tablet formulation with ideal characteristics such as good flow properties, high compressibility, pharmaceutically acceptable disintegration pattern and low friability for the mentioned applications.

US2011013476 relates to a process of production of a tabletting excipient comprising filler/binding agent, flow regulating agent, disintegrant and sodium stearyl fumarate as lubricant. The specified components i.e. filler, binding agent, flow regulating agent, disintegrant and lubricant is ideally produced through granulation in the fluid bed. In this process the lubricant is sprayed on co-granulated components. The said prior art requires addition of lubricant during formulation by spray drying, Furthermore the process requires heating and use of solvents contributing to increased risk during processing. The process is involves additional number of steps.

WO201107496 (EP2512455) pertains to a co-processed excipient composition suitable for tabletting comprising one filler-binder, disintegrant, lubricant which is subjected to granulation. The lubricant is co-processed in the matrix, and the composition is provided with a lactose coat.

Article from Pharm-Tech on PanExcea MHC300G: The performance excipient of the prior art is a co-processed excipient containing three main component of a solid dosage formulation: filler, binder, and disintegrant. Ibuprofen formulation

exemplified therein requires addition of lubricant/glidants during the compression with the active.

US5840769 relates to direct tabletting aid comprising A) 75-98% by weight of powdered cellulose suitable for tabletting, B) 1-15% by weight of soluble polyvinylpyrrolidone, and C) 0.5-10% by weight of crosslinked insoluble polyvinylpyrrolidone.

Although, filler-binder/adhesive-disintegrant mixture is available as ready to be mixed with API, and compressed; none of these have been able to provide tablets with uniform distribution, good flow properties, high compressibility, disintegration pattern and low friability.

Thus there exists an unmet need in the pharmaceutical state-of-art to develop new and improved excipient compositions to be in contour with ever advancing tabletting technology that result in tablet with desirable characteristics; more so the disintegration pattern.

The inventors of the present invention have surprisingly and successfully prepared an excipient composition which when mixed with wide range of active pharmaceutical ingredients (API or APIs) result in oral dosage forms with good flow properties, high compressibility, pharmaceutically acceptable disintegration pattern and low friability. The excipient compositions of the present invention are thus intended to provide a tablet with such physical characteristic as well as dissolution and disintegration pattern; and processes for preparation thereof that result in low operation cost and time to an appreciable extent; less equipment handling; decrease in skilled/unskilled labor; as well as reduction in over head expenses.

OBJECTS OF THE INVENTION

An object of the present invention is to develop a simple and efficient manufacturing for preparing solid dosage form.

An object of the present invention is to provide an excipient composition for direct compression.

An object of the present invention is to provide an excipient composition that result in solid dosage form with good flow properties, high compressibility, pharmaceutically acceptable disintegration pattern and low friability.

Another object of the present invention is to provide one-step preparation of final oral dosage form.

Further object of the present invention is to reduce operation time per batch.

Yet another object of the present invention is to economize the tabletting procedure and thereby the production cost.

SUMMARY OF THE INVENTION

According to an aspect of the present invention there is provided an excipient composition for tabletting comprising:

a. 65 to 90 % w/w diluent;
b. 0 to 1.0 % preservatives;
c. 5 to 20 % w/w binders/adhesive;
d. 0 to 20% w/v disintegrant
e. 0.5 to 15 % w/w lubricant
f. 0 to qs (optionally) organoleptic additives.

According to another aspect of the present invention there is provided a process of preparation of the excipient composition comprising steps:

i. mixing diluents, binder, antiadherents for 10 minutes in rapid mixer granulator;
ii. preparation of a binder paste solution in stem jacketed paste making kettle and cooling the resultant paste to 40 to 45° Celsius;
iii. granulation of step i mixture alongwith the binder paste of step ii;
iv. wet milling the granules of step iii;
v. drying the granules of step iv;
vi. sifting the dried granules through 20# mesh using vibrator sifter;

vii. milling the sieved granules through multi-mill;

viii. adding lubricant sifted through 40# to granules of step vii in an octagonal blender.

DESCRIPTION OF THE INVENTION

The excipient composition of the present invention is manufactured in very controlled technique in which all the key components are incorporated in appropriate ratio so as to ensure a consistent product with uniform distribution, good flow properties, high compressibility, required disintegration pattern and low friability.

According to another aspect of the present invention there is provided an excipient composition without any active pharmaceutical ingredient.

The excipient composition of the present invention comprises all ingredients required for granulation except API. This includes diluents, binders, anti adherents, disintegrant as per the need and physicochemical characteristics of the API to be formulated. The excipient composition is manufactured by wet granulation with diluents, binders, disintegrating agents and lubricants. The excipient from various categories of diluents such as MCC, lactose, Starch, Di-Calcium Phosphate, etc; binders like Pre-Gelatinized Starch, Starch, PVP of different grades, gelatin, gums etc; lubricants such as talc, Mg Stearate, Colloidal Silicon Dioxide etc; disintegrating agents such as Sodium Starch Glycolate (SSG), Cross Carmellose Sodium, Crosspovidone, Starch etc; and organoleptic additives such as coloring agents, flavoring agents, sweeteners etc,

The excipient composition is instrumental in determining the release of the drug. The excipient compositions of the present invention are therefore made available in specific grades. The different grades of excipient compositions are accordingly provided as direct compression excipient; sustained release excipient, dispersible tablet excipient, and dispersible tablet excipient;

The excipient composition of the present invention aids direct compression when mixed with the API. The excipient composition of the present invention consists of

all ingredients required in pre-determined amounts for granulation. This includes diluents, binders, anti adherents, lubricants and disintegrant as per the need and properties of the API to be formulated.

The excipient composition of the present invention provides the final dosage form with excellent flowability and compressibility, uniform particle size distribution, and better dilution potential. The excipient compositions of the present invention are applicable to low dosage formulation, if used in geometrical proportion gives excellent drug distribution.

The use of the excipient composition of the present invention invariably leads to minimizing operational cost, as many operations such as wet granulation, drying, sifting, dry screening etc can be eliminated. The formulation therefore is only blending of the API with the excipient composition of the present invention followed by compression. This thus results in one-step operation to make granules ready for compression. It reduces man power, electric consumption, and above all the production time. This also minimizes the inventory as against many ingredients.

The present invention offers an advantage of moisture and heat free processing, and hence can be used for moisture sensitive and thermo-labile drugs successfully.

According to an aspect of the present invention, yield can be improved as operations are minimized resulting into controlled losses.

The excipient composition of the present invention is available as:

I. **Excipient composition-DC: (Direct Compression Excipient):** The excipient composition- Direct Compression (DC) is a tailor made, pre granulated excipient for specific Active Pharmaceutical Ingredient (API). It is manufactured by controlled process of granulation to get uniform, homogeneous mixture of ingredients having good flow properties, high compressibility and required disintegration pattern. The direct compression excipient composition of the present invention is as follows:

a) 75 to 85 % w/w diluents;

b) 0 to 1.0 % w/w Preservatives

c) 5 to 15 % w/w binders/adhesive;

d) optionally disintegrant q.s. % w/w; and

e) 0.5 to 5 % w/w lubricant.

One or more diluents / bulking agents may be selected from Hypromellose (Hydroxypropyl Methylcellulose),Ethylcellulose, Hydroxypropyl Cellulose ,Hydroxy ethyl Cellulose, Carboxy methyl cellulose Calcium, Tribasic Calcium Phosphate, Calcium Carbonate, Dibasic Calcium Phosphate Dihydrate, Microcrystalline Cellulose, Dextrose, Kaolin, Lactose, Magnesium Carbonate, Magnesium Oxide, Mannitol, Sorbitol, Pregelatinised Starch, Sugar Spheres, or Starch/ Polyvinyl Alcohol.

One or more binders may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethyl Cellulose, Carbomer, Gelatin, Starch, Pregelatinised Starch, PVPK 30 (Povidone), Xanthan Gum, Carboxymethylcellulose Sodium, or Hydroxypropyl Cellulose.

One or more disintegrants may be selected from Bentonite, Croscarmellose Sodium, Crospovidone, Magnesium Aluminum Silicate, Polacrilin Potassium, Sodium Starch Glycolate, Stearyl Alcohol USP, PVPK (Povidone), Carboxy methylcellulose Sodium or Starch.

One or more lubricants and anti-adherents may be selected from Calcium Stearate, Magnesium Stearate, Sodium Stearyl Fumarate, Stearyl Alcohol, Cetyl Alcohol, Stearic Acid, Talc, Colloidal Silicon Dioxide or Glyceryl Monostearate.

One or more preservatives may be selected from Sodium Ethyl Paraben, Sodium Methyl Paraben, Sodium Propyl Paraben, Potassium Benzoate, Sodium Benzoate, Butyl Paraben, Butylated Hydroxyanisole, Butylated Hydroxytoluene, Chlorobutanol, Sorbic Acid, Potash Alum, Potassium Metabisulfite, or Sodium Metabisulphite

Excipient composition-DC is best-suited for:

- Low-dose drugs such as hormones, steroids etc.

- High dosage of API with good compressibility e.g. Aspirin Norfloxacin, Alprazolam etc.

II Excipient composition sustained release (SR) tablets: The SR excipient is a tailor made, pre granulated excipient for specific Active Pharmaceutical Ingredient (API). It is manufactured by controlled process of granulation to get uniform, homogeneous mixture of ingredients having good flow properties, high compressibility and required disintegration pattern. The excipient composition for sustained release tablet is as follows:

a. 70 to 90 % w/w diluent;
b. 0 to 1.0 % preservatives
c. 5 to 15 % w/w binders/adhesive;
d. 2 to 10 % w/w lubricant;
e. 0 to qs disintegrant.

One or more Diluents / Bulking agents may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethylcellulose, Hydroxypropyl Cellulose, Hydroxy ethyl Cellulose, Carboxy methyl cellulose Calcium, Tribasic Calcium Phosphate, Calcium Carbonate, Dibasic Calcium Phosphate Dihydrate, Microcrystalline Cellulose, Dextrose, Kaolin, Lactose, Magnesium Carbonate, Magnesium Oxide, Mannitol, Sorbitol, Pregelatinised Starch, Sugar Spheres, Starch, or Polyvinyl Alcohol.

One or more Binders may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethyl Cellulose, Carbomer,Gelatin, Starch, Pregelatinised Starch, PVPK 30 (Povidone), Xanthan Gum, Carboxymethylcellulose Sodium or Hydroxypropyl Cellulose.

One or more disintegrants may be selected from Bentonite, Croscarmellose Sodium, Crospovidone, Magnesium Aluminum Silicate, Polacrilin Potassium, Sodium Starch

Glycolate, Stearyl Alcohol USP, PVPK (Povidone), Carboxymethylcellulose sodium or starch

Lubricants and anti-adherents Calcium Stearate / Magnesium Stearate / Sodium Stearyl Fumarate / Stearyl Alcohol /Cetyl Alcohol / Stearic Acid / Talc / Colloidal Silicon Dioxide / Glyceryl Monostearate.

One or more preservatives may be selected from Sodium Ethyl Paraben, Sodium Methyl Paraben, Sodium Propyl Paraben, Potassium Benzoate, Sodium Benzoate, Butyl Paraben, Butylated Hydroxyanisole, Butylated Hydroxytoluene, Chlorobutanol, Sorbic Acid, Potash Alum, Potassium Metabisulfite, or Sodium Metabisulphite.

Excipient composition - Direct Compression Excipient have been formulated for: Sustained release products e.g. diltiazem, isosorbide 5 Mono Nitrate (ISMN), Glicazide, Diclofenac Sodium, Ambroxol, And Triglyceryl Nitrate.

III. Excipient composition for Dispersible tablets (DT): DT Direct Compression Excipient is a tailor made, pre granulated excipient for specific Active Pharmaceutical Ingredient (API) as per the requirement. It is manufactured by controlled process of granulation to get uniform, homogeneous mixture of ingredients having good flow properties, high compressibility and required disintegration pattern. The excipient composition for dispersible tablet is as follows:

a. 65 to 85 % w/w diluent;
b. 0 to 1.0 % w/w Preservatives
c. 5 to 20 % w/w binders/adhesive;
d. 5 to 20 % w/w disintegrant; and
e. 2 to 10 % w/w lubricant
f. 0 to qs organoleptic additives

One or more diluents / Bulking may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethylcellulose, Hydroxypropyl Cellulose, Hydroxy ethyl Cellulose,

Carboxy methyl cellulose Calcium, Tribasic Calcium Phosphate, Calcium Carbonate, Dibasic Calcium Phosphate Dihydrate, Microcrystalline Cellulose, Dextrose, Kaolin, Lactose, Magnesium Carbonate, Magnesium Oxide, Mannitol, Sorbitol, Pregelatinised Starch, Sugar Spheres, Starch, or Polyvinyl Alcohol

One or more Binders may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethyl Cellulose, Carbomer, Gelatin, Starch, Pregelatinised Starch, PVPK 30 (Povidone), Xanthan Gum, Carboxymethylcellulose Sodiumor Hydroxypropyl Cellulose.

One or more Disintegrants may be selected from bentonite, Croscarmellose Sodium, Crospovidone, Magnesium, Aluminum Silicate, Polacrilin Potassium, Sodium Starch Glycolate, Stearyl Alcohol USP, PVPK (Povidone), Carboxymethylcellulose Sodium or Starch.

Lubricants and anti-adherents may be selected from calcium Stearate, Magnesium Stearate, Sodium Stearyl Fumarate, Stearyl Alcohol, cetyl Alcohol, Stearic Acid, Talc, Colloidal Silicon Dioxide, or Glyceryl Monostearate.

One or more preservatives may be selected from Sodium Ethyl Paraben, Sodium Methyl Paraben, Sodium Propyl Paraben, Potassium Benzoate, Sodium Benzoate, Butyl Paraben, Butylated Hydroxyanisole, Butylated Hydroxytoluene, Chlorobutanol, Sorbic Acid, Potash Alum, Potassium Metabisulfite or Sodium Metabisulphite

The excipient composition is best-suited for dispersible tablet formulations with low disintegration time such as Roxithromycin, Nimesulide. The resultant dispersible tablets achieve disintegration time from about 'less than 3 minutes' to about 'less than 1 minute'.

IV. Excipient composition for Specialized (SP) preparation: The excipient composition is suitable for moisture sensitive or hygroscopic drugs e.g. Ranitidine HCl. The excipient composition for moisture sensitive or hygroscopic API is as follows:

a. 70 to 85 % w/w diluent;

b. 0 to 1.0 % preservatives
c. 5 to 20 % w/w binders/adhesive;
d. optionally, a disintegrant qs % w/w;
e. 2 to 15 % w/w lubricant;
f. optionally, organoleptic additives qs % w/w

One or more Diluents / Bulking may be selected from hypromellose (Hydroxypropyl Methylcellulose), Ethylcellulose, Hydroxypropyl Cellulose, Hydroxy ethyl Cellulose, Carboxy methyl cellulose Calcium, Tribasic Calcium Phosphate, Calcium Carbonate, Dibasic Calcium Phosphate Dihydrate, Microcrystalline Cellulose, Dextrose, Kaolin, Lactose, Magnesium Carbonate, Magnesium Oxide, Mannitol, Sorbitol, Pregelatinised Starch, Sugar Spheres, Starch, or Polyvinyl Alcohol.

One or more Binders may be selected from Hypromellose (Hydroxypropyl Methylcellulose), Ethyl Cellulose, Carbomer, Gelatin, Starch, Pregelatinised Starch, PVPK 30 (Povidone), Xanthan Gum, Carboxymethylcellulose Sodium, or Hydroxypropyl Cellulose.

One or more disintegrants may be selected from Bentonite, Croscarmellose Sodium, Crospovidone, Magnesium Aluminum Silicate, Polacrilin Potassium, Sodium Starch Glycolate, Stearyl Alcohol USP, PVPK (Povidone), Carboxymethylcellulose Sodium or Starch.

Lubricants and anti-adherents may be selected from Calcium Stearate, Magnesium Stearate, Sodium Stearyl Fumarate, Stearyl Alcohol, Cetyl Alcohol, Stearic Acid, Talc, Colloidal Silicon Dioxide or Glyceryl Monostearate.

One or more Preservatives may be selected from Sodium Ethyl Paraben, Sodium Methyl Paraben, Sodium Propyl Paraben, Potassium Benzoate, Sodium Benzoate, Butyl Paraben, Butylated Hydroxyanisole, Butylated Hydroxytoluene, Chlorobutanol, Sorbic Acid, Potash Alum, Potassium Metabisulfite, or Sodium Metabisulphite

Flavors and sweeteners can be incorporated in the formulation as needed;

One or more flavours and/or sweeteners may be selected from Ethyl Vanilline, Vanilline, Ethyl Maltol, Lemon Oil, Orange Oil, Peppermint Oil, Rose Oil, Spearmint Oil, Mix Fruit flavour, Pineapple flavour, Banana flavour, Cardamon Oil, Cinnanon Oil, Clove Oil, Fennel USP, Citric Acid, Ginger, Honey purified sucrose, Manitol, Aspartame, Neotame, Sorbitol or Glucose.

Preparation of Compressed tablets with Excipient Composition of the present invention:

Excipient composition of present invention

⇩

Active Ingredients

⇩

Dry mixing

⇩

Compression to tablets

Manufacturing Process -Flow Chart (Refer Figure –I)

MANUFACTURING PROCEDURE:

1. Granulation:

1.1 Load all the Raw material (sifted through 40#) in the rapid mixer granulator (RMG) serially as mention in the Quantitative formula of respective product. Dry mix all the contents for 20 mins at fast speed.

1.2 Preparation of Binder Paste/ Solution: Prepare Binder Paste / Solution as per the Percentage mention in the Quantitative formula of respective product in A steam jacketed paste making kettle. Cool the paste to 40 -45°C

1.3 Wet Granulation: Add the Binder paste to the same rapid mixer granulator under constant stirring at high speed and continue stirring for 10 min. Check for

thorough mixing and if required continue mixing for further 10 min. (Note the additional Quantity of water used if required liters)

1.4 Wet Milling: Mill the wet dough in the Multi Mill using Mesh No.: 8 mm (required mesh size)

2. Drying: Dry the granules in Fluid Bed Dryer

3. Dry Milling:

3.1 Sifting: Pass the dried material through 20 # mesh using vibratory sifter. Collect the passed material in double polyethylene lined plastic HDPE drums/or S.S. containers.

3.2 Milling: Collect the granular material above the sieve and pass through Multi-mill: Using Screen 1 mm at fast medium speed. (Knives forward.) (Required sieve);

3.3 Granules ready for lubrication: Weigh granules of Step 3.1 and 3.2. Calculate the yield.

4. Lubrication and Final Blending: Transfer the granules of step No. 3.3 to an octagonal blender, add disintegrating/ super disintegrating agents & lubricants (sifted through 40# before use) & mixed thoroughly for 10 min

Advantages over conventional methods of Granulation

- No granulation
- Reduced Operation time per batch
- Higher yield than normal granulation
- Energy saving in terms of drying and other granulation steps.
- Reduced chances of contamination.
- Moisture and heat-free processing hence better drug stability
- Elimination of hazardous steps (non aqueous granulation)

Advantages over Direct Compression Grade Excipients

- Customized Formulations according to the characteristics of API
- No need of other excipients or pretreated excipients (Single inventory).
- Better Flowability.

- Better Hardness and Low Friability.
- Economical.

Examples:

Reference is made in detail to the preferred embodiments of the invention. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. In addition, it will be appreciated by one of the skill in the art, that the technology of the present invention may be applicable to other APIs as well.

Qualitative and quantitative examples of excipient composition of the present invention:

Sr. no	Formula	Percentage
1	**EXCIPIENT COMPOSITION DC-01**	
	MICROCRYSALLINE CELLULOSE (MCC)	29.29
	LACTOSE	24.5%
	STARCH	29.4 %
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL (PREGELATINIZED STARCH)	4.9 %
	STARCH (PASTE)	9.8 %
	TALC	1.0 %
	COLLOIDAL SILICON DIOXIDE	0.5 %
	MAGNESIUM STEARATE	0.5 %

2	**EXCIPIENT COMPOSITION DC-02**	
	LACTOSE	48.39%
	STARCH	38.8 %
	COLL SIO2	2.9 %
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	STARCH (PASTE)	2.4 %
	STARCH	3.9%
	TALC	2.0%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MG STEARATE	1.0%

3	**EXCIPIENT COMPOSITION DC-RD02**	
	DI BASIC CALCIUM PHOSPHATE (DCP)	49.89%
	LACTOSE	20.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	STARCH (PASTE)	22.0%
	GELATIN (PASTE)	4.0%
	PVP K-30	4.0%

4	**EXCIPIENT COMPOSITION DC-RD03**	
	DI BASIC CALCIUM PHOSPHATE (DCP)	38.89%
	MCC	39.0%
	LACTOSE	10.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL (PREGELATINIZED STARCH)	5.0%
	STARCH (PASTE)	5.0%
	TALC	1.0 %
	COLLOIDAL SILICON DIOXIDE	0.5 %
	MAGNESIUM STEARATE	0.5 %

5	**EXCIPIENT COMPOSITION DC-RD04**	
	DI BASIC CALCIUM PHOSPHATE (DCP)	77.89%
	LACTOSE	10.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL (PREGELATINIZED STARCH)	5.0%
	STARCH (PASTE)	5.0%
	TALC	4.0%
	COLLOIDAL SILICON DIOXIDE	1.0 %
	MAGNESIUM STEARATE	0.5 %

6	***EXCIPIENT COMPOSITION DC-RD05***	
	DI BASIC CALCIUM PHOSPHATE (DCP)	41.0%
	MCC	41.89%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	STARCH (PASTE)	10.0%
	PVP K-30	5.0%
	TALC	1.0 %
	COLLOIDAL SILICON DIOXIDE	0.5 %
	MAGNESIUM STEARATE	0.5 %

7	**EXCIPIENT COMPOSITION -DT**	
	MCC	26.29%
	LACTOSE	22.0%
	STARCH	26.4 %
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	4.4 %
	STARCH (PASTE)	8.8%
	SODIUM CROSS CARMELLOSE	8.0%
	SSG	2%
	TALC	1%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MAGNESIUM STEARATE	0.5%

8	**EXCIPIENT COMPOSITION DT-01**	
	MCC	26.29%
	LACTOSE	22.0%
	STARCH	26.4 %
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	4.4%
	STACH (PASTE)	8.8 %
	CROSPOVIDONE	10%
	TALC	1%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MAGNESIUM STEARATE	0.5%

9	**EXCIPIENT COMPOSITION DT-02**	
	MCC	26.89%
	LACTOSE	22.5%
	STARCH	27.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	4.5%
	STARCH (PASTE)	9.0%
	STARCH	3.0%
	CROSPOVIDONE	5%
	TALC	1%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MAGNESIUM STEARATE	0.5%

10	**EXCIPIENT COMPOSITION DT-03**	
	MCC	25.49%
	LACTOSE	21.2%
	STARCH	25.5%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	4.2%
	STARCH (PASTE)	8.5%
	STARCH	3.0%
	SODIUM CROSS CARMELLOSE	8.0%
	SSG	2.0%
	TALC	1.0%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MAGNESIUM STEARATE	0.5%

11	**EXCIPIENT COMPOSITION DT-04**	
	MCC	26.39%
	LACTOSE	22.5%
	STARCH	26.7%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	4.4%
	STARCH (PASTE)	8.9%
	STARCH	3.0%
	CROSPOVIDONE	5%
	TALC	1%
	COLLOIDAL SILICON DIOXIDE	0.5%
	MAGNESIUM STEARATE	0.5%
	SODIUM LAURYL SULPHATE	1.0%

12	**EXCIPIENT COMPOSITION SR (A)**	
	MCC	54.89%
	ETHYL CELLULOSE (EC)	1.5%
	HPMC K100	30%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	STARCH (PASTE)	3.75%
	PVP K-30	3.75%
	TALC	2.0%
	COLLOIDAL SILICON DIOXIDE	2.0 %
	MAGNESIUM STEARATE	2.0 %

13	**EXCIPIENT COMPOSITION SR (B)**	
	MCC	49.89%
	EC	1.5%
	HPMC K100	35.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	STARCH (PASTE)	3.75%
	PVP K-30	3.75%
	TALC	2.0%
	COLLOIDAL SILICON DIOXIDE	2.0 %
	MAGNESIUM STEARATE	2.0 %

14	**EXCIPIENT COMPOSITION SR (C)**	
	MCC	45.0%
	EC	1.5%
	HPMC K100	40.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABENS	0.01%
	TARCH (PASTE)	3.75%
	PVP K-30	3.75%
	TALC	2.0%
	COLLOIDAL SILICON DIOXIDE	2.0 %
	MAGNESIUM STEARATE	2.0 %

15	**EXCIPIENT COMPOSITION SR (D)**	
	MCC	25.0%
	EC	1.5%
	HPMC K100	35.0%
	HPMC K4	25.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABENS	0.01%
	TARCH (PASTE)	3.75%
	PVP K-30	3.75%
	TALC	2.0%
	COLLOIDAL SILICON DIOXIDE	2.0 %
	MAGNESIUM STEARATE	2.0 %

16	**EXCIPIENT COMPOSITION SR**	
	MCC	30.37%
	EC	0.96%
	HPMC K-4	52.38%
	SODIUM METHYL PARABEN	0.10%

	SODIUM PROPYL PARABEN STARCH (PASTE) PVP K-30 TALC COLLOIDAL SILICON DIOXIDE MAGNESIUM STEARATE	0.01% 7.63% 2.86% 1.9% 1.9 % 1.9 %

17	**NOVOPOWER SR (E)** MCC EC HPMC K-100 PVP K-30 TALC COLL. SIO2 MAGNESIUM STEARATE STARCH	 50% 1.5% 35.0% 4.5% 2.0% 2.0 % 2.0 % 3.0%

18	**NOVOPOWER SR (F)** MCC EC HPMC K-100 PVP K-30 TALC COLL. SIO2 MAGNESIUM STEARATE STARCH HPMC K-100 10.0%	 50.0% 1.5% 25.0% 4.5% 2.0% 2.0 % 2.0 % 3.0% 10.0%

19	**NOVOPOWER SR (G)** MCC EC HPMC K-100 PVP K-30 TALC COLL. SIO2 MAGNESIUM STEARATE STARCH	 32.66% 0.96% 52.38% 5.0% 2.0% 2.0 % 2.0 % 3.0%

20	**NOVOPOWER SR (H)**	
	MCC	32.66%
	EC	0.96%
	HPMC K-100	42.38%
	PVP K-30	5.0%
	TALC	2.0%
	COLL. SIO2	2.0 %
	MAGNESIUM STEARATE	2.0 %
	STARCH	3.0%
	HPMC K-4	10.0%

21	**NOVOPOWER SR (I)**	
	MCC	65.0%
	EC	1.5%
	HPMC K-100	15.0%
	PVP K-30	4.5%
	TALC	2.0%
	COLL. SIO2	2.0 %
	MAGNESIUM STEARATE	2.0 %
	STARCH	3.0%
	HPMC K-100	5.0%

22	**EXCIPIENT COMPOSITION SP1RD1**	
	MCC	65.89.0%
	COLLOIDAL SILICON DIOXIDE	10.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%
	PREGEL	5.0%
	STARCH (PASTE)	7.0%
	SODIUM STARCH GLYCOLATE (SSG)	2.0%
	CROSS CARMELLOSE NA	8.0%
	TALC	1.0 %
	COLLOIDAL SILICON DIOXIDE	0.5 %
	MAGNESIUM STEARATE	0.5 %

23	**EXCIPIENT COMPOSITION SP2RD1**	
	MCC	37.89%
	LIGHT MAGNESIUM OXIDE	25.0%
	STARCH	10.0%
	PREGEL	5.0%
	SODIUM METHYL PARABEN	0.10%
	SODIUM PROPYL PARABEN	0.01%

	STARCH (PASTE)	12.0%
	SODIUM STARCH GLYCOLATE (SSG)	8.0%
	TALC	1.0 %
	COLLOIDAL SILICON DIOXIDE	0.5 %
	MAGNESIUM STEARATE	0.5 %

TECHNICAL ADVANCEMENT AND ECONOMIC SIGNIFICANCE:

Example no. 1: Ofloxacin-100mg, Tablet

Ofloxacin-100mg, Tablet A/Weight-300 mg, B. size 1.0 lac using conventional process		
Product	Material	Cost (Rs.)
Oflaxacin	10 kg	--
MCC	6.00 kg	441
Lactose	3.600 kg	414
Starch	4.000 kg	80
PVP K-30	0.200 kg	66
Sodium methyl paraben	0.160 kg	80
Sodium propyl paraben	0.060 kg	27
Talc	3.400 kg	54.4
Magnesium stearate	2.400 kg	168
Colloidal silicon dioxide	0.200 kg	96.4
Total	30 kgs	1426.8 (a)

Other Expenses:

Electric charges, Manpower, water charges for 1 strip (10 tabs.) = 0.75 Rs

Therefore Electric charges, Manpower, water charges for 1 tablet = 0.075 Rs.

Therefore Electric charges, Manpower, water charges for 1 Lac Tabs (1 Batch) = 7,500 Rs (b)

Total cost for 1 batch of 1 lac Tabs. = (a) + (b) = 8926.8 Rs.

Total cost for Daily 5 batches (5 lac Tabs.) = 44,634 Rs.

Total cost for Monthly 150 batches (1.5 crore Tabs.) = 13,39,020 Rs.

Ofloxacin-100mg, Tablet A/Weight-300 mg, B. size 1.0 lac Using Excipient Composition process

Product	Material	Cost(Rs.)
Oflaxacin	10 kg	--
Excipient Composition DC -01	20 kg	4040
Total	30 kgs	4040

Other expenses:

Total cost for 1 batch of 1 lac Tablets. = (a) + (b) = 4540Rs.

Total cost for Daily 5 batches (5 lac Tablets.) = 22,700 Rs.

Process time comparison:

Process time with the use of Excipient Composition DC -01		Process time for conventional process	
Process	Time	Process	Time
Dispensing	30 mins	Dispensing	1Hrs,40 mins
Man power Required - 2	--	Man power Required – 3	--
-	--	Auto sifting	40 mins
Auto Blend	15 mins	Paste Preparation Auto	45 mins
--	--	Auto granulation	35 mins
--	--	FBD Dry	30 mins
--	--	FBD Dry Again	25 mins
--	--	Auto wet screening	15 mins
--	--	Auto sifting	25 mins
--	--	Auto blending	15 mins
Total Time Required	45 mins	Total Time Required-	5 Hrs 30 mins

Benefits:

1. The Total time saving per Batch is 4 Hrs. 30 mins. Approx. So, that you can manufacture more batches
2. Total cost saving per batch is Rs.4400 Approx
3. Total cost saving per month (for app.150 batches) is Rs. 6,60,000 Approx
4. Total cost saving per annum is Rs. 79,20,000 Approx

Example no. 2: Ranitidine 168 mg, Tablet

Ranitidine 168 mg, Tablet A/Weight-500 mg, B. Size 1.0 lac Using conventional process		
Product	Material	Cost (Rs.)
Ranitidine	16.8 kg	--
MCC	9.2 00kg	676.2
Starch	4.800 kg	145.92
Lactose	12.400 kg	1757.7
PVP K-30	0.200 kg	200
Sodium methyl paraben	0.200 kg	56
Sodium propyl paraben	0.080 kg	29.2
Talc	3.200 kg	51.2
Magnesium stearate	1.500 kg	289.8
Total	50 kgs	3206.02(a)

Other Expenses:

Electric charges, Manpower, water charges for 1 strip (10 tabs.) = 0.75 Rs

Therefore Electric charges, Manpower, water charges for 1 tablet = 0.075 Rs.

Therefore Electric charges, Manpower, water charges for 1 Lac Tabs (1 Batch) = 7,500 Rs (b)

Total cost for 1 batch of 1 lac Tabs. = (a) + (b) = 10,706.2 Rs.

Total cost for Daily 5 batches (5 lac Tabs.) = 53,531 Rs.

Total cost for Monthly 150 batches (1.5 crore Tabs.) = 16,05900 Rs.

Ranitidine 168 mg, Tablet A/Weight-500 mg, B. Size 1.0 lac Using Excipient Composition SP-01		
Product	Material	Cost (Rs.)
Ranitidine	16.800 Kg	
Excipient Composition SP-01	33.200 Kg	9960
Total	50 kgs	9960 (a)

Other Expenses:

Electric charges, Manpower, water charges for 1 strip (10 tabs.) = 0.05 Rs

Therefore Electric charges, Manpower, water charges for 1 tablet = 0.005 Rs.

Therefore Electric charges, Manpower, water charges for 1 Lac Tabs (1 Batch) = 500 Rs (b)

Total cost for 1 batch of 1 lac Tabs. = (a) + (b) = 10460 Rs.

Total cost for Daily 5 batches (5 lac Tabs.) = 52300 Rs.

Total cost for Monthly 150 batches (1.5 crore Tabs.) = 15, 69,000 Rs.

Process time comparison

Process time with the use of Excipient Composition SP 01		Process time for conventional process	
Process	Time	process	Time
Dispensing	30 mins	Dispensing	1Hrs,40 mins
Man power Required - 2	--	Man power Required - 3	
--	--	Auto sifting	40 mins
Auto Blend	15 mins	Paste Preparation Auto	45 mins
--	--	Auto granulation	35 mins
--	--	FBD Dry	30 mins
--	--	FBD Dry Again	25 mins
--	--	Auto wet screening	15 mins
--	--	Auto sifting	25 mins
--	--	Auto blending	15 mins
Total Time Required	45 mins	Total Time Required	5 Hrs 30 mins

Benefits

1) Your Total time saving per Batch is 4 Hrs. 30 mins. Approx. So, that you can manufacture more batches.

2) Total cost saving per batch is 246 Rs. Approx.

3) Total cost saving per month is 36900 Rs. Approx.

4) Total cost saving per annum is 4,42,800 Rs. Approx.

Example no. 3: Multi-Vitamin Oral Solid tablets (Beplex Forte-357.1 mg)

Beplex Forte-357.1 mg, Tablet A/Weight- 682.5 mg (Excluding Coating), B.size- 1.0 lac , Using conventional process		
Product	Material	Cost(Rs.)
Thiamine Mononitrate IP	1 kg	--

Riboflavine	1 kg	--
Nicotinic acid IP	2.5 kg	--
Niacinamide IP	7.5 kg	--
Pyridoxine hydrochloride IP	*0.300 kg*	--
Calcium pantothenate IP	5 kg	--
Folic acid IP	0.150 kg	--
Vitamin B12 IP	0.001 kg	--
Vitamin C IP	15.00 kg	--
Biotin USP	0.026 kg	--
Light Magnesium oxide IP/MG	3.24 kg	--
MCC	6.400 kg	470
Lactose monohydrate	8.600 kg	989
starch	2.800 kg	56
Pregelatinised starch	5.400 kg	459
PVP K-30	2.600 kg	858
Sodium methyl paraben	0.800 kg	400
Sodium propyl paraben	0.400 kg	180
TALC	2.800 kg	43.68
Colloidal silicon dioxide	1.200 kg	289.8
calcium stearate	2.600 kg	325
TOTAL	68.25 KG	4070.48 (a)

Other expenses:

Electric charges, Manpower, water charges for 1 strip (10 tabs.) = 0.75 Rs

Therefore Electric charges, Manpower, water charges for 1 tablet = 0.075 Rs.

Therefore Electric charges, Manpower, water charges for 1 Lac Tabs (1 Batch) = 7,500 Rs (b)

Total cost for 1 batch of 1 lac Tabs. = (a) + (b) = 11,570 Rs.

Total cost for Daily 5 batches (5 lac Tabs.) = 57,852 Rs.

Total cost for Monthly 150 batches (1.5 crore Tabs.) = 17,35,560 Rs.

Multi Vitamin oral solids (Beplex Forte-357.1 mg) Tablet A/Weight- 682.5 mg (Excluding Coating), Batch.size- 1.0 lac , Using Excipient composition SP-01		
Product	Material	Cost (Rs.)

Thiamine Mononitrate IP	1 kg	--
Riboflavine	1 kg	--
Nicotinic acid IP	2.5 kg	--
Niacinamide IP	7.5 kg	--
Pyridoxine hydrochloride IP	0.300 kg	--
Calcium pantothenate IP	5 kg	--
Folic acid IP	0.150 kg	--
Vitamin B12 IP	0.001 kg	--
Vitamin C IP	15.00 kg	--
Biotin USP	0.026 kg	--
Light Magnesium oxide IP/MG	3.24 kg	--
Excipient composition SP-01	32.54 Kgs.	6573.08
Total	68.25 KG	9762 (a)

Other expenses

Electric charges, Manpower, water charges for 1 strip (10 tabs.) = 0.05 Rs

Therefore Electric charges, Manpower, water charges for 1 tablet = 0.005 Rs.

Therefore Electric charges, Manpower, water charges for 1 Lac Tabs (1 Batch) = 500 Rs (b)

Total cost for 1 batch of 1 lac Tabs. = (a) + (b) = 10,262 Rs.

Total cost for Daily 5 batches (5 lac Tabs.) = 51310 Rs.

Total cost for Monthly 150 batches (1.5 crore Tabs.) = 15, 39,300 Rs.

Process time comparison:

Process time with the use of excipient composition SP-01		Process time for conventional process	
Process	Time	process	Time
Dispensing	30 mins	Dispensing	1Hrs,40 mins
		Man power Required - 3	
Man power Required - 2		Auto sifting	40 mins
Auto Blend	15 mins	Paste Preparation Auto	45 mins
--	--	Auto granulation	35 mins
--	--	FBD Dry	30 mins
--	--	FBD Dry Again	25 mins

--	---	Auto wet screening	15 mins
--	--	Auto sifting	25 mins
--	--	Auto blending	15 mins
Total Time Required	45 mins	Total Time Required-	5 Hrs 30 mins

Benefits:

1) Total time saving per Batch is 4 Hrs. 30 mins. (Approximately); this enables accommodation of more batches

2) Total cost saving per batch is 1308 Rs. (Approx).

3) Total cost saving per month is 1,96,200 Rs. (Approx).

4) Total cost saving per annum is 23,54,400 Rs. (Approx).

Conclusion:

The comparisons data shown in aforesaid examples emphasizes that with excipient composition of the present invention; the pharmaceutical industry can save on processing time as well other overhead expenses such as electric charges, manual labor, water charges, operational cost, etc. The excipient composition of the present invention economizes the whole tabletting procedure pharmaceutical technology to an appreciably high extent. This benefits the end user to save on manufacturing costs without compromising on the quality of production; increases the productivity of the infrastructure; prevent wear and tear of the equipment; manufacturing cost minimized as a whole. This would invariably result in reduction production/manufacturing cost of the tablets and the economical benefit would also pass on the end-user, the patient.

We Claim:

1. An excipient composition for tabletting comprising:
    a. 65 to 90 % w/w diluent;
    b. 0 to 1.0 % preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. 0 to 20% w/v disintegrant
    e. 0.5 to 15 % w/w lubricant
    f. 0 to qs organoleptic additives.

2. The excipient composition for tabletting as claimed in claim 1 for dispersible tablet comprising:
    a. 65 to 85 % w/w diluent;
    b. 0 to 1.0 % w/w preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. 5 to 20 % w/w disintegrant; and
    e. 2 to 10 % w/w lubricant.
    f. 0 to qs organoleptic additives.

3. An excipient composition for tabletting as claimed in claim 1 for direct compression of moisture sensitive or hygroscopic active pharmaceutical ingredients comprising:
    a. 70 to 85 % w/w diluent;
    b. 0 to 1.0 % preservatives
    c. 5 to 20 % w/w binders/adhesive;
    d. optionally a disintegrant q.s. % w/w
    e. 2 to 15 % w/w lubricant
    f. optionally, organoleptic additive q.s. % w/w

4. A tabletting process for preparation of excipient composition comprising steps:
   i. mixing diluents, binder, anti-adherents for 20 minutes in rapid mixer granulator;
   ii. preparation of a binder paste solution in stem jacketed paste making kettle and cooling the resultant paste to 40 to 45 degree Celsius;
   iii. granulation of step i mixture along with the binder paste of step ii;
   iv. wet milling the granules of step iii;
   v. drying the granules of step iv;
   vi. sifting the dried granules through 20# mesh using vibrator sifter;
   vii. milling the sieved granules through multi-mill;
   viii. adding lubricant sifted through 40# to granules of step vii, in an octagonal blender.

5. The excipient composition for tabletting as claimed in any of the preceding claims wherein the diluent is selected from MCC, HPMC, ethyl cellulose, lactose, starch, di-calcium phosphate or mixtures thereof.

6. The excipient composition for tabletting as claimed in any of the preceding claims wherein the binders or adhesive is selected from pre-gelatinized starch, Starch, polyvinyl pyrrolidine of different grades, gelatin, gums or mixtures thereof.

7. The excipient composition for tabletting as claimed in any of the preceding claims wherein one or more disintegrants are selected from sodium starch glycolate (SSG), croscarmellose sodium, crospovidone, fumed silicon dioxide, starch or mixtures thereof.

8. The excipient composition for tabletting as claimed in any of the preceding claims wherein lubricant is selected from talc, magnesium stearate, fumed silica, colloidal silicon dioxide or mixtures thereof.

9. The excipient composition for tabletting as claimed in any of the preceding claims wherein organoleptic additive may be colorant, flavoring agent or sweetener.

Dated this the 14th day of June 2013

Mythili Venkatesh
Of S. Majumdar & Co
(Applicant's Agent)