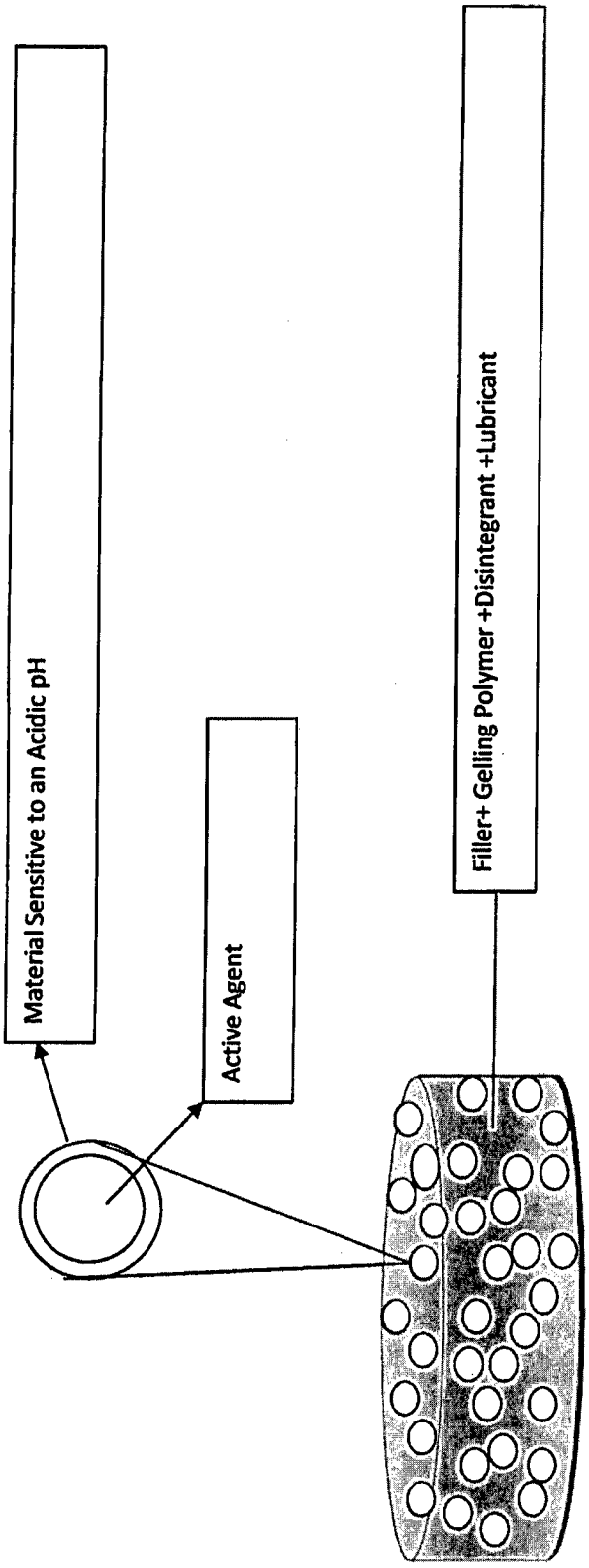

Material Sensitive to an Acidic pH
Active Agent
Filler+ Gelling Polymer +Disintegrant +Lubricant

FIGURE 1

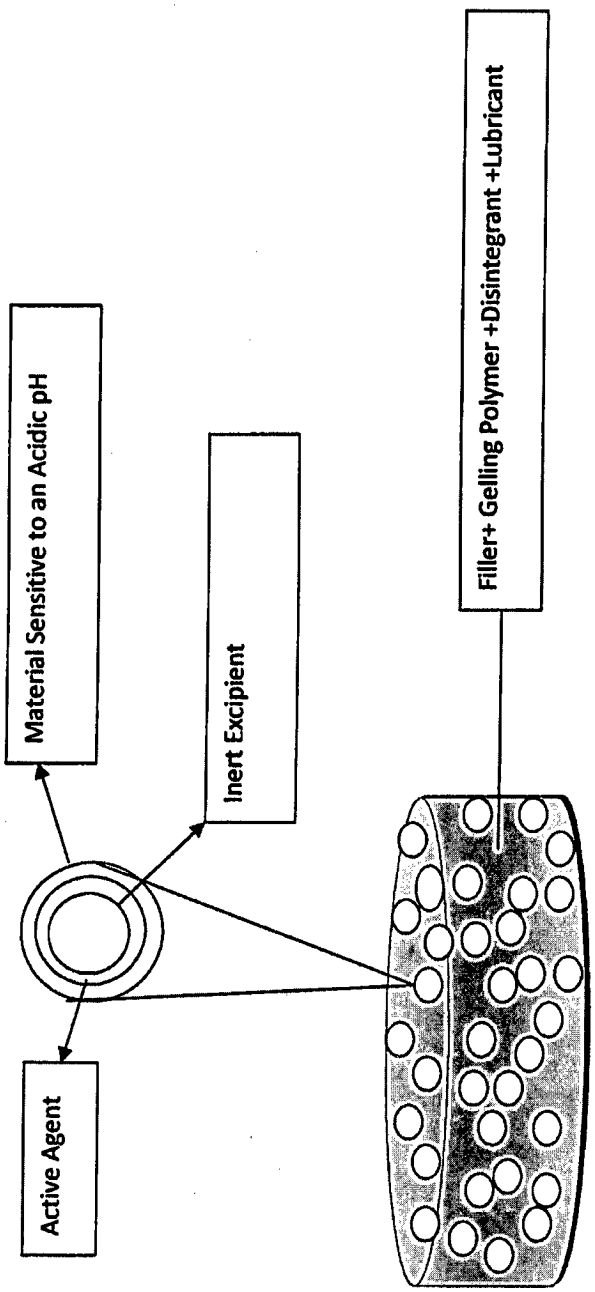

Material Sensitive to an Acidic pH
Inert Excipient
Filler+ Gelling Polymer +Disintegrant +Lubricant
Active Agent

FIGURE 2

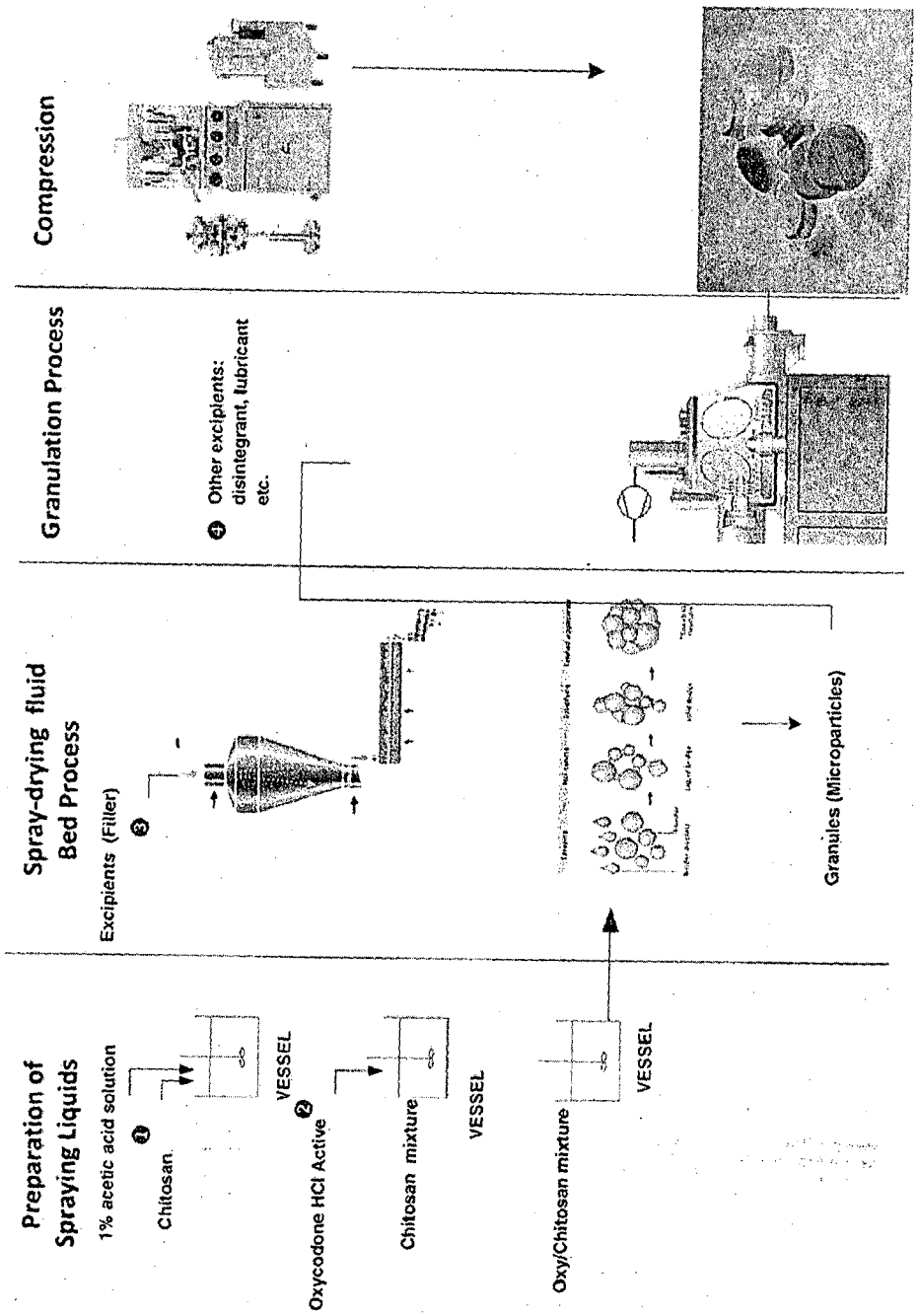

Preparation of Spraying Liquids
1% acetic acid solution
Chitosan
VESSEL
Oxycodone HCl Active
Chitosan mixture
VESSEL
Oxy/Chitosan mixture
VESSEL
Spray-drying fluid Bed Process
Excipients (Filler)
Granules (Microparticles)
Granulation Process
Other excipients: disintegrant, lubricant etc.
Compression

FIGURE 3

FIGURE 4

Human Bioavailability Results: Mean (SD) Plasma Oxycodone Concentration-Time Profile (Linear Scale) – Fed PK Summary (E PO vs RLD)

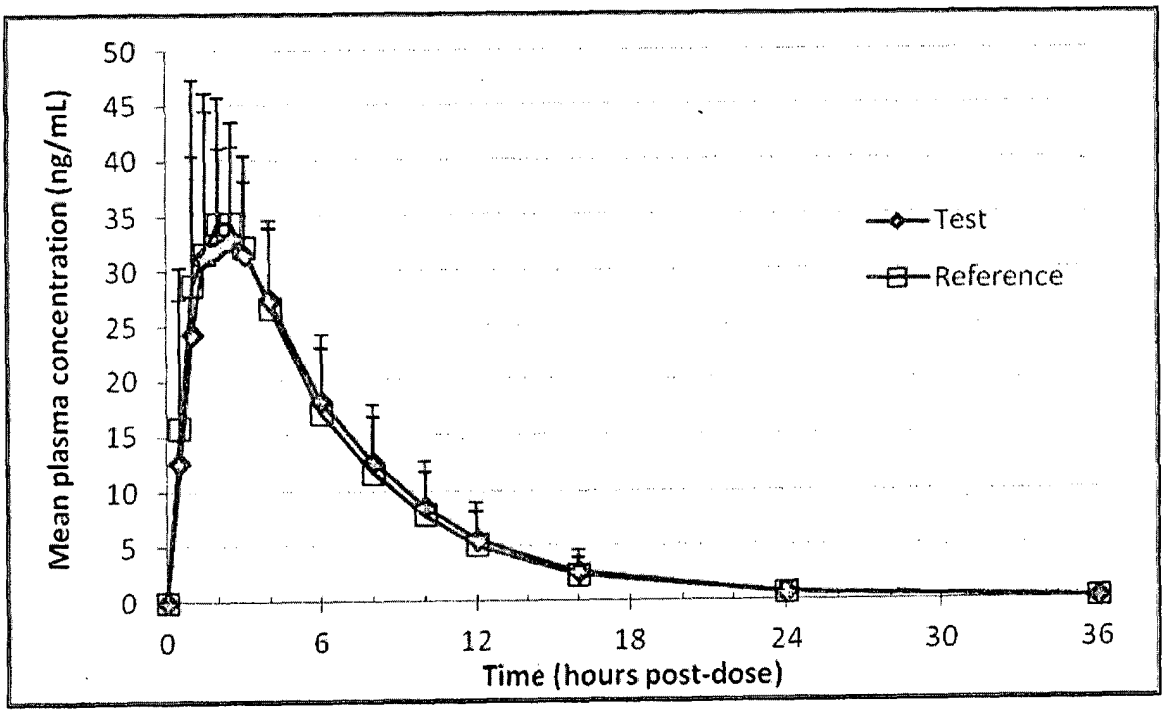


FIGURE 5

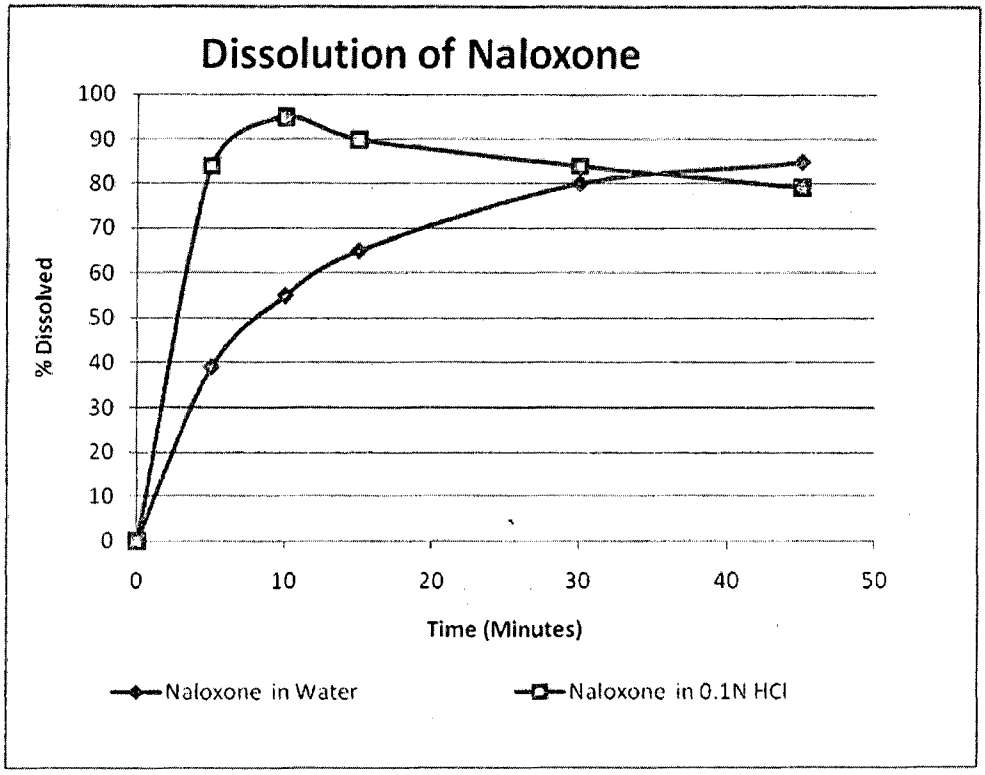

Dissolution of Naloxone
% Dissolved
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
Time (Minutes)
Naloxone in Water
Naloxone in 0.1N HCl

FIGURE 6

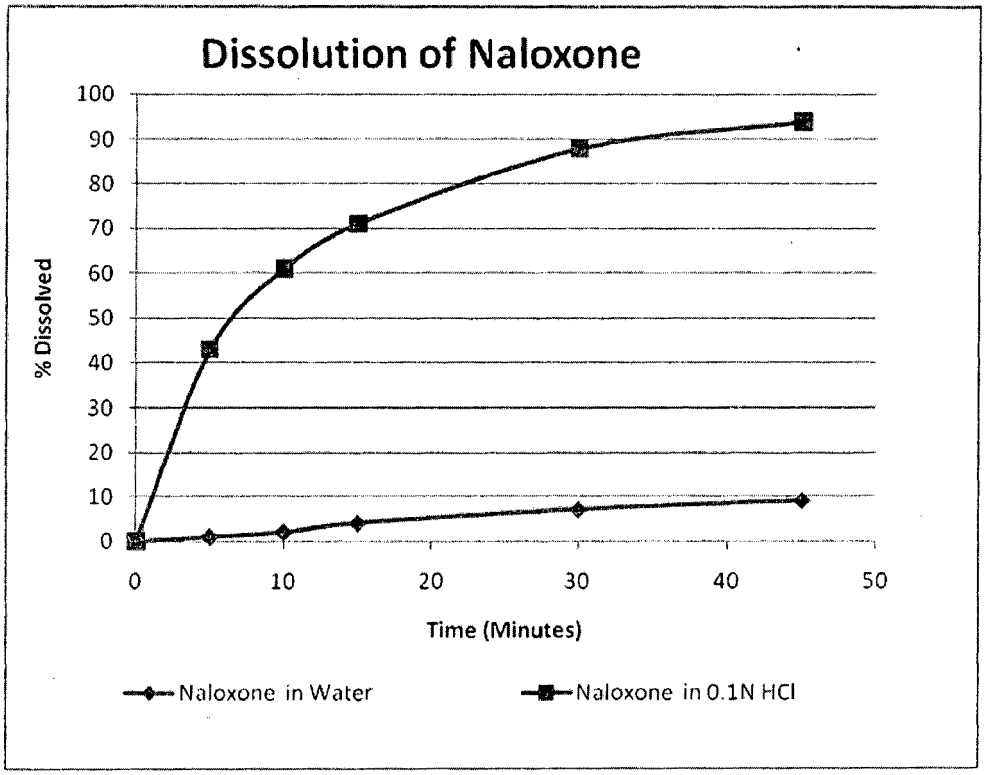

Dissolution of Naloxone
% Dissolved
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
Time (Minutes)
Naloxone in Water
Naloxone in 0.1N HCl

FIGURE 7

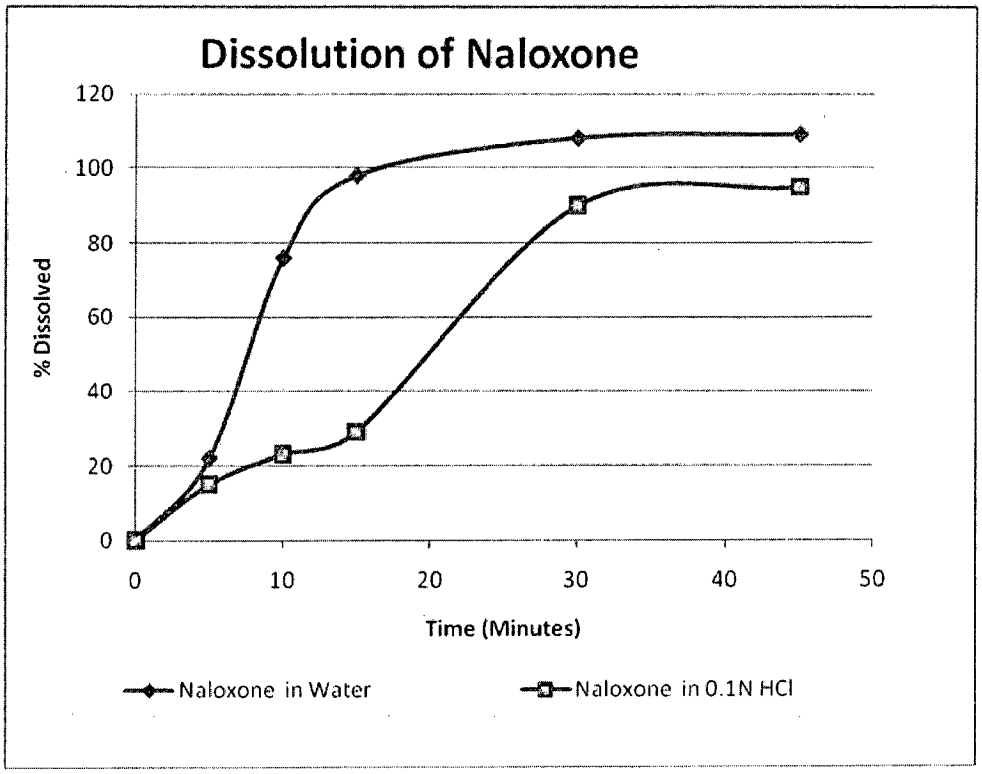

Dissolution of Naloxone
120
100
80
60
40
20
0
% Dissolved
0
10
20
30
40
50
Time (Minutes)
Naloxone in Water
Naloxone in 0.1N HCl

FIGURE 8

Stage Layering of Naloxone on Substrate APAP Granules

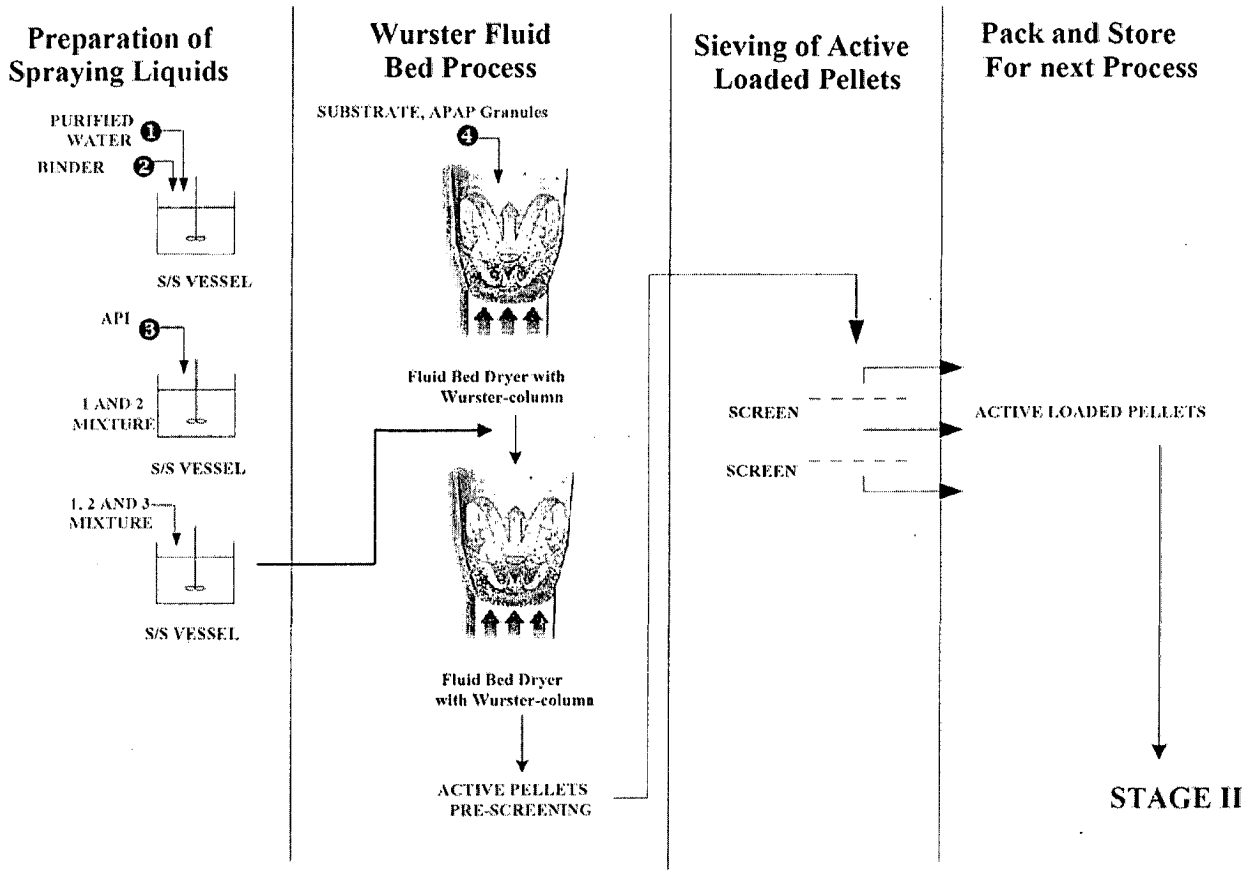


FIGURE 9

Processing Stage II - Production of Naloxone Loaded Polymer Coated Pellets

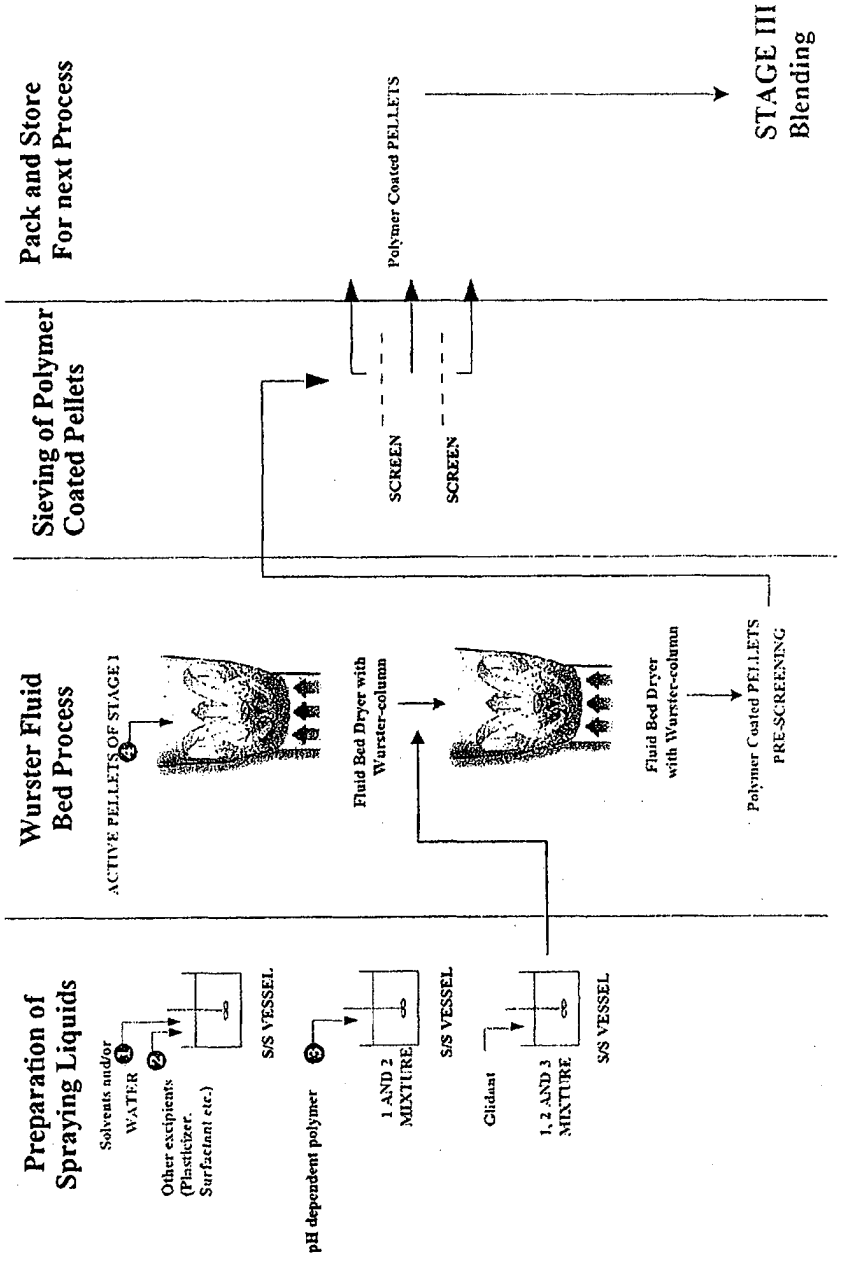
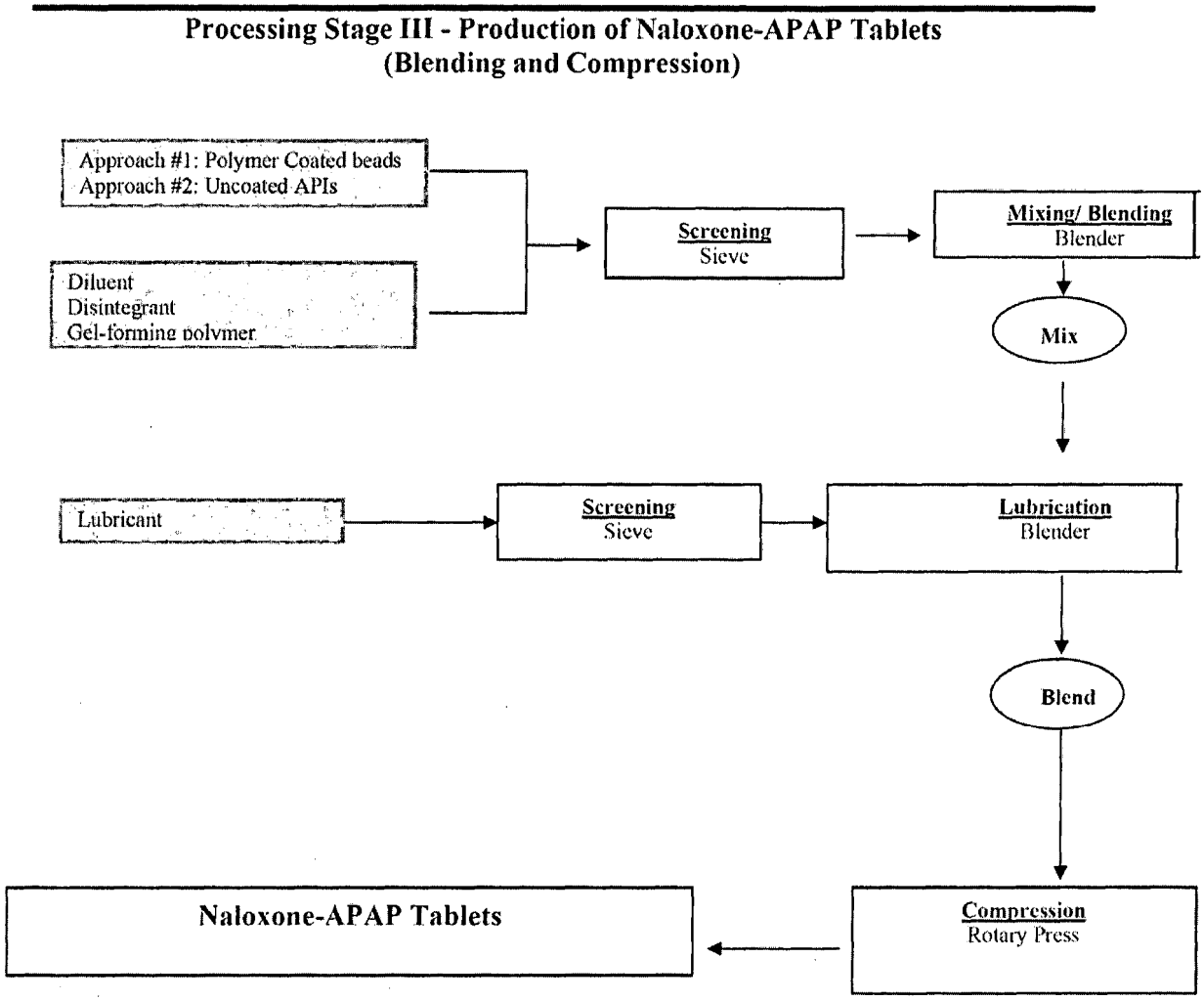


FIGURE 10


Processing Stage III - Production of Naloxone-APAP Tablets
(Blending and Compression)
Approach #1: Polymer Coated beads
Approach #2: Uncoated APIs
Diluent
Disintegrant
Gel-forming polymer
Screening
Sieve
Mixing/ Blending
Blender
Mix
Lubricant
Screening
Sieve
Lubrication
Blender
Blend
Compression
Rotary Press
Naloxone-APAP Tablets

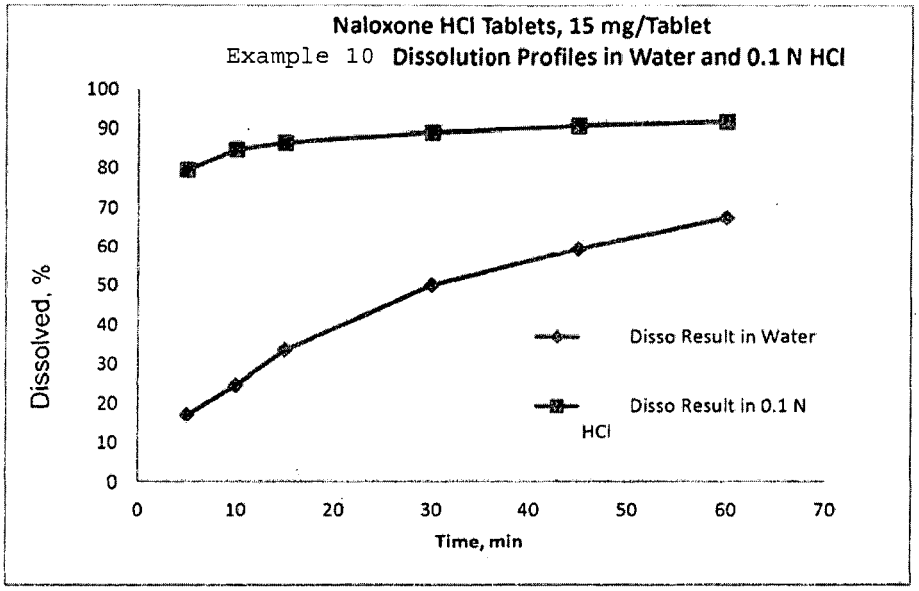

Naloxone HCl Tablets, 15 mg/Tablet
Example 10 Dissolution Profiles in Water and 0.1 N HCl
Dissolved, %
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
Time, min
Disso Result in Water
Disso Result in 0.1 N HCl

FIGURE 11