Acetaminophen, Salicylamide, Caffeine, and Codeine Tablets (150 mg/200 mg/50 mg/10 mg)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Salicylamide	200.00
150.00	2	Acetaminophen powder	150.00
50.00	3	Caffeine anhydrous	50.00
10.00	4	Codeine phosphate	10.00
130.00	5	Starch (maize)	130.00
5.00	6	Gelatin powder	5.00
8.00	7	PVP K30	8.00
1.00	8	Aerosil 200	1.00
30.00	9	Starch (maize)	30.00
–	10	Water, purified	300 mL
10.00	11	Talc powder	10.00
19.00	12	Starch (maize), dried	19.00
1.00	13	Aerosil 200	1.00

Manufacturing Directions

Note: The binding solution is prone to microbiological growth. Use only freshly prepared and properly stored solution.

1. Charge item 6 and about 25 mL of item 10 into a vessel to dissolve item 6. Mix for 10 minutes.
2. In a separate vessel, add and dissolve items 9 and 7 in about 12 mL of water.
3. Charge item 5 into a vessel; add about 40 mL of cold item 10 and 20 mL of hot (70–75°C) water, after first dissolving in cold water.
4. In a separate vessel, charge items 1 to 5 after passing them through a 630-μm sieve. Mix for 5 minutes at medium speed.
5. Add binding solution from step 3 and mix at medium speed. Continue until a satisfactory mass is obtained.
6. Dry the wet mass in a fluid-bed dryer at 50°C for 45 minutes to 1.5% to 2.5% LOD.
7. Pass the dried granules through a 1.5-mm sieve.
8. Load granules in a cone blender and mix for 5 minutes.
9. Add items 11 to 13 (passed through a 500-μm sieve) to blender, and blend for 5 minutes.
10. Compress into 634-mg tablets, using 12.7-mm flag bevel-edge punches.

Acetaminophen Sustained-Release Tablets

Manufacturing Directions

1. 300 g of acetaminophen and 60 g of hydroxypropylmethyl cellulose were dissolved in a mixture of 720 g of methanol and 720 g of dichloromethane.
2. 300 g of Celphere 102 (mean particle diameter of approximately 127 μm, particle diameter of approximately 50–150 μm) was introduced to a fluidized bed granulator and coated with the solution by the side spraying method (spraying liquid volume 14 g/min, spraying air pressure 3 kg/cm^2, product temperature 32°C, and inlet temperature 45°C) to obtain acetaminophen particles.
3. Separately, 48 g of ethyl cellulose and 12 g of hydroxypropylmethyl cellulose were dissolved in a mixture of 57 g of purified water and 1083 g of methanol.
4. Acetaminophen particles (300 g) were introduced to a fluidized bed granulator and coated with this solution by side spraying (spraying liquid volume of 8 g/min, spraying air pressure of 3 kg/cm^2, product temperature of 38°C, and inlet temperature of 67°C) to obtain sustained-release fine particles.
5. 66 g of these sustained-release fine particles and 314.25 g mannitol that had been pulverized by a pin mill pulverizing device were granulated (spraying liquid volume 15 g/min, spraying air pressure of 1.1 kg/cm^2, product temperature of 30°C, inlet temperature of 38°C, and spraying cycle of 30-seconds spraying and 30-seconds drying) with an aqueous 30% w/w solution containing 67.5 g of maltose in a fluidized bed granulator to obtain the final composition.
6. After further mixing 2.25 g of magnesium stearate with the composition that was obtained, 450-mg tablets containing 25-mg acetaminophen per tablet were made under a tableting pressure of 25 kg/punch and an initial hardness of 2.0 kPa, using a rotary tableting machine.
7. Next, these tablets were kept for 24 hours while heating and humidifying at 25°C/75% RH, using a thermostatic chamber at constant humidity. Then they were dried for 3 hours at 30°C and 40% RH.
8. The tablets that were obtained showed a hardness of 3.5 kPa and disintegration time in the buccal cavity of 12 seconds.