

mesh screen and were then used for the following physical tests. Particle size distribution was determined using a sieving method. A weighed amount (400 g) of granulated excipients was placed on the first sieve of a nest of US Standard 8-in, stainless-steel sieves (mesh sizes of 24, 32, 42, 60, 80, and 115) arranged in order of decreasing aperture size. The nest of sieves was subjected to vibration for at least 5 min, or until no apparent change in weight was observed. After sieving, the amount retained on each sieve was weighed, and the cumulative percent retained on each sieve was calculated.

An A.B.D. Fine Particle Characteristics Measuring Instrument (Tsutsui Scientific Instruments, Tokyo, Japan) was used to determine the bulk and tapped densities, and repose angle of the powders. Carr's index¹⁶ was calculated as the ratio of the difference between tapped density and bulk density to tapped density. The average of 3 determinations was reported.

Preparation of Solid Dispersion Systems

A solvent method was employed to prepare solid dispersion systems for nifedipine. PVP and HPMC were selected as the water-soluble polymers. After dissolving nifedipine and PVP (K30, 1:1 w/w) or HPMC (5 cps, 1:1 or 1:3 w/w) in a suitable volume of an acetone/water mixture, the solvent mixture was completely evaporated in a forced-air convection oven at a temperature of 50–60 °C. Dried residues were ground with a coffee mill, and granules passing an 80-mesh sieve were collected. These solid dispersion samples were then stored in desiccators protected from light until use.

Analysis by Differential Scanning Calorimetry

A differential calorimeter (DSC Thermal Analyst 2000) was used to determine the phase transition temperature for the solid dispersion systems of nifedipine with PVP (1:1), HPMC (5 cps, 1:1), and HPMC (5 cps, 1:3). A heating rate of 10 °C/min was employed from 30 to 250 °C in an atmosphere of nitrogen with samples placed in aluminum pans. Indium was used as the calibration standard.

Preparation and Characterization of Nifedipine Matrix Tablets

Nifedipine controlled-release tablets of the matrix

type were prepared by direct compression as follows: nifedipine or its solid dispersion (equivalent to 20 mg nifedipine) and 1 talc were blended initially with the granulated excipients prepared above. The mixture was then compressed to form tablets using a Carver laboratory press (Fred S. Carver, USA) utilizing a standard 7.5-mm concave punch and die system with a 1-ton compression force. The press was set at a rotation speed of 2 mm/min; a dwell time of 0.6 s was used during compression. A total weight equivalent to 20 mg of nifedipine was prepared for each tablet. Friability was evaluated by dropping 10 tablets 100 times using a Roche Friabilator (Model AE-20, Aikho Engineering, ROC). The crushing strength of tablets was measured with a hardness tester (Euweka TB21). The thickness was determined using a thickness tester (Mitutoyo).

Dissolution Test

The USP paddle method was used to measure dissolution rates. The dissolution medium was pH 1.2 simulated gastric fluid maintained at 37.0 ± 0.5 °C with the addition of 1% (w/v) Tween 80. Samples were withdrawn at fixed time intervals and analyzed for the drug using a UV method. The detection wavelength for UV analysis was 350 nm, and the calibration curve was constructed to determine the drug concentration in the samples.

RESULTS AND DISCUSSION

It was previously reported that matrix tablets produced with particles formed by granulated lactose, dicalcium phosphate with film-forming polymers, either Eudragit RS-30D, and RL-30D or Surelease, exhibited satisfactory friability of less than 1 except those prepared from lactose particles granulated with a low percentage of ethylcellulose and from plain lactose granules.¹⁷ Although friability can be improved by increasing the percentage of film-forming polymers in the granule formulations, the wet mass after adding granulation solution can become too viscous to evenly distribute the granulating agent among the particles. Two other studies also found that it was necessary to add HPMC (Metolose 60-SH, 50 cps) to improve the cohesion of granulated excipients when using a low percentage of film-forming polymer in granule form.