Abstract

Losartan potassium (LP) is a type of medicine called an Angiotensin II receptor antagonist. It works by preventing the action of a hormone in the body called angiotensin II. Angiotensin II normally acts on special receptors in the body, with two main results. It causes the peripheral blood vessels to narrow, and it also stimulates the production of another hormone called aldosterone. Aldosterone causes salt and water to be retained by the kidneys, which increases the volume of fluid in the blood vessels. LP blocks the receptors that angiotensin II acts on, and so prevents its actions. The main result of this is that the peripheral blood vessels are allowed to widen, which means that there is more space and less resistance in these blood vessels. This helps lower blood pressure.

The present invention comprises a pharmaceutical solid dosage form having a first layer with an immediate release property and a second layer with a sustained release property. Each of these layers contains LP, with the ratio of the LP in the first layer to the second layer being in the range of from about 10:90 to about 12:88 by weight. Another aspect of the present invention is a method of treatment comprising administering to a patient in need thereof pharmaceutical solid dosages form wherein the total amount of LP is available in a therapeutic level for longer period.

Method of formulation is divided in three major stages.

Stage I: LP is encapsulated into Eudragit RS 100 (ERS) and Eudragit RL 100 (ERL) microspheres. The microspheres were prepared using solvent evaporation technique with an ultimate aim of prolonging drug release. Six formulations were prepared using different drug/polymer ratio. The effects of polymer type and polymer/ drug ratios on the size, surface morphology, encapsulation efficiency and the release characteristics of the microspheres were examined. The formulation containing drug/polymer ratio 1:5 in which the ratio between the two polymers (ERS: ERL) is 4:1 was found to be the most appropriate with respect to encapsulation efficiency (94.43 % ± 0.277), drug loading (19.58 % ± 0.417), batch yield (80.40 % ± 1.712), particle size (204.23 ± 8.438) and having highest correlation coefficient (0.9909) amongst all formulation thus providing a desired drug release characteristics. At the optimum stirring speed of 750 rpm, best spherical shaped particles with good surface characteristics were obtained, which were distributed over the size range of 120-270 μm. This proposed method has been successfully used to prepare batches of microspheres having high encapsulation efficiencies.

Stage II: The Sustained release layer containing prepared microspheres, diluents, binder and lubricants were mixed uniformly and passed through sieve # 80, then compressed on single station tablet punching machine using 8 mm round and flat punches with hardness between 4-5 kg cm\(^{-2}\).

Stage III: IR layer containing LP, super disintegrating agent, diluents and lubricant were mixed uniformly and compressed over CR layered tablet with hardness between 5-7 kg cm\(^{-2}\) to obtain bi-layer tablet.

Post compression parameters like hardness, thickness, friability, weight variation test and drug content complied with pharmacopeial limit for the tablets. FTIR and Differential Scanning Calorimetry study revealed no chemical interaction between drug, polymers and excipients used. Pre-compression parameters like angle of repose, bulk density, tapped density, Carr’s index and Hausner’s ratio were within the limits. Post compression parameters like hardness, thickness, friability, weight variation test and drug content complied with pharmacopeial limit for the tablets. In-vitro release studies were carried out using USP XXIV type II (paddle method) dissolution apparatus at 75 rpm by taking 900 ml phosphate buffer pH 6.5 for the time period at 37±0.5°C. The extent of swelling was measured in terms of percentage weight gain by the tablets. Bi-layer tablets of LP showed an initial burst to provide the loading dose of the drug, followed by the controlled release for 24h, indicating a promising potential of the LP t as a bi-layer table.