passing the tiny gap of the homogenizer; the static pressure on the water decreases below the vapor pressure of water; the water starts boiling at room temperature, leading to the formation of gas bubbles; and at the exit of the gap, the gas bubbles implode. The implosion shock waves disintegrate the drug particles to drug nanoparticles. Further improvement on nanoparticle production includes homogenization in the nonaqueous phases or with reduced water content to produce more pronounced cavitation at higher temperatures. The chemical stability of the drugs is less impaired when homogenizing in nonaqueous or water-reduced media at low temperatures. The drug powder is dispersed in a nonaqueous medium (e.g., polyethylene glycol [PEG] 600 and Miglyol 812) or in a water-reduced mixture (e.g., water-ethanol), and the presuspension is homogenized in a piston-gap homogenizer. A suitable machine for lab scale is the Micron Lab 40 (APV Deutschland GmbH, Lübeck, Germany). Ostwald ripening occurs because of different saturation solubilities in the vicinity of very small and large particles. The particles produced are relatively homogeneous. The differences in the size, in combination with the generally poor solubility of the drug nanoparticles, are sufficiently low to avoid Ostwald ripening. Aqueous drug nanoparticle suspensions generally prove to be physically stable for several years.

The application of micronization and nanonization increases the surface area, leading to an increased dissolution rate, according to the Noyes–Whitney equation. However, this is only one aspect. The dissolution pressure is a function of the curvature of the surface that is much stronger for a curved surface of nanoparticles. For a size less than approximately 1–2 μm, the dissolution pressure increases distinctly, leading to an increase in saturation solubility. In addition, the diffusional distance $h$ on the surface of drug nanoparticles is decreased, thus leading to an increased concentration gradient $(Cs-Cx)/h$. The increase in surface area and concentration gradient leads to a greater increase in the dissolution velocity compared with a micronized product. In addition, the saturation solubility is also increased, even though it is a thermodynamic parameter; the increase in solubility occurs as the supersaturation stage is reached. Saturation solubility and dissolution velocity are important parameters affecting the bioavailability of orally administered drugs. From this, nanoparticles have the potential to overcome these limiting steps.

Nanoparticle-based products are likely to have some unique characteristics: general adhesiveness of nanoparticles to the gut wall; adhesion to the gut wall being a reproducible process, thus minimizing variation in drug absorption, increase in dissolution velocity overcoming this rate-limiting step; and an additional increase in the saturation solubility, leading to an increased concentration gradient between the gut and blood. Orally administered drug nanoparticles can increase the bioavailability and can be the only tool available to achieve sufficient bioavailability with poorly soluble drugs. However, the possibility of faster absorption may have drawbacks, both from pharmacology and stability in the gut. For intravenous administration, the drug nanoparticles should possess a bulk population in the nanometer range by simultaneously having a low microparticle content, that is, especially particles larger than 5 μm, which can cause capillary blockade. The homogenization process yields a product with a minimized content of particles larger than 1 μm. Intravenous administration of drug nanoparticles allows the achievement of sufficient blood levels and finds good application in the evaluation of new compounds. In addition, toxicologically critical excipients, such as Cremophor EL used in Taxol formulations can be avoided when stabilizing the drug nanoparticles with accepted emulsifiers, for example, lecithin and