These range from treatment of cold symptoms to head aches to allergies to gastrointestinal discomfort, and so on. Brands like Tylenol and Advil have become household names. Once tablets or capsules are taken whole, they dissolve in the digestive tract and are then distributed throughout the body in the blood to reach their target area. However, some active pharmaceutical ingredients are not soluble. In fact, more than 40% of new chemical entities developed in the pharmaceutical industry have little or no solubility in water (due to the non-polar or very small polar nature of the chemical composition of the drug). Sometimes, effective drugs cannot be taken through tablets or capsules because of their inability to dissolve in water and disperse in the body. Considering the magnitude of drugs that are not completely soluble in water, a method of administering these drugs is needed to utilize the full advantages of new innovation in the pharmaceutical field. These insoluble drugs can still be used by administering them throughout the body with a different method that has been made possible with modern technological improvements.

One of the simpler ways of administering the drug is to simply change its physical size. By grinding drugs into powder form, we increase the surface area to volume ratio which can increase the solubility potential. Smaller particle size may create improved absorption through increased solubility and improve delivery efficiency. However, for completely insoluble drugs, milling the drug or ingredient down to a powder with particle sizes in the nanometer range (around twenty to thirty nanometers) can also create particles small enough to directly distribute throughout the body. This nano suspension process effectively eliminates the need for the dissolution of the drug after it has entered the body. Then, by suspending the powder in a saline solution that has a similar composition to that in the human body, the drug can be delivered directly into the blood stream through an injection or aerosol spray. While there are other methods of applying a nano suspension, using media milling for micronizations is the simplest and most cost-effective. Creating smaller particle sized APIs not only creates benefits for insoluble drugs, but can also make the administration of other drugs more effective. However, when milling down drugs to nanometer particle size, it is important to keep in mind that the significant amounts of physical and possible thermal stress that the drugs are put under may cause degradation.

When considering this method, zeta potential plays a crucial role in whether the process will work. Zeta potential is a measure of charge in a suspension that characterizes attractive and repulsive forces between suspended particles. A zeta potential value closer to 0 mV means that the particles are likely to be attracted to each other, agglomerate, and possibly settle out of the suspension, while values further away from 0 mV indicate that the particles are likely to repel each other and remain in suspension. Zeta potential can be modified by pH or additives, such as surfactants or certain salts. A drug nano suspension with low zeta potential may cause the particles to agglomerate, or clump, in the saline and inhibit the ability of the drug to be properly and evenly distributed or prevent entry into target cells. This can reduce or eliminate the desired therapeutic effect. Therefore assessing the zeta potential of a drug is a crucial step when considering this process.

With new technology that can assess particle size and zeta potential, this technique of administering drugs is easier and more precise than it’s ever been. Insoluble? No problem!