Strategies to improve the stability of solid dispersion drug products

The drugs which are having poor water solubility they often show poor oral bioavailability due to the low levels of absorption. Solid dispersion is defined as dispersion of one or more active ingredients (hydrophobic) in an inert carrier (hydrophillic). It is enhance the solubility and dissolution rate of the poorly water soluble drug by reducing the particles size, improved wettability and porosity, and changing the drug crystalline state into a more preferable amorphous state.

- Physical instability.
- SDs show changes in crystallinity and decreased dissolution rate with aging.
- Due to their thermodynamic instability, SD is sensitive to temperature and humidity during storage.

Amorphous state can enhance the solubility of crystalline drug as the lack of crystal structure reduces the energy needed to overcome the lattice energy during dissolution process.

These factors can promote phase separation and crystallization of SD by increasing the overall molecular mobility, decreasing the glass transition temperature (Tg) or disrupting interactions between the drug and carrier, resulting in a decreased solubility and dissolution rate of the drug.

Active pharmaceutical ingredients (API) properties

- The biopharmaceutical drug classification system (BCS) is a useful tool for decision-making.
- Physicochemical properties for designing ASD of a drug molecule are the glass transition temperature, glass formation propensity, hydrogen bond donor/acceptor in the structure, melting temperature, and thermo-chemical stability as well as the dose of drug.

Carrier selection

- Physicochemical properties of polymers which should be considered during formulation development include; glass transition temperature, aqueous solubility, molecular weight, hygroscopicity and potential for stabilization via intermolecular interactions between the polymer and the API.
- In general, polymer stabilize amorphous drug in solid dispersion by decreasing their molecular mobility, through increasing the Tg of the miscible mixture (polymer-amorphous solid dispersion), and form intermolecular interactions with the API.

Manufacture method selection

Two major distinct processes are used to prepared solid dispersion: melting and solvent evaporation. Both solvent evaporation and melting processes have their own advantages and drawbacks that should be considered in order to select the most suitable manufacturing process.