Amphoteric molecules contain both acidic and basic functional groups and can exist in neutral or zwitterionic state. Many of these compounds can undergo zwitterion to neutral, and vice versa switch in solution by adjusting the pH. Control over these transformations is important because neutral and zwitterionic forms of amphoteric molecules exhibit different properties. A very few examples were reported for the stabilization of these transformations in solid state by solvent or additives. In pharmaceutical point of view the control over these transformations of drugs are very important, because zwitterionic forms having higher solubility over neutral forms, whereas neutral forms having higher membrane permeability. There is thus a trade-off between high permeability and low solubility for the neutral form, or high solubility and low permeability of zwitterionic forms. A stable neutral form in the solid-state with high solubility and bioavailability together with superior permeability will provide a general solution to drug pharmaceutics. In this context, we report a novel strategy for the stabilization of neutral form of amphoteric drug sparfloxacin (SPX) in solid state by supramolecular amino-phenol synthon recognition. SPX immediately transforms to the zwitterion trihydrate when contacted with water. Hence to stabilize the neutral form of SPX, we selected GRAS (generally recognised as safe) coformers, and more specifically the parabens, which are known for their antioxidant properties and used as excipients in tablet formulation. Our rationale to cocrystallize SPX-paraben cocrystals, was guided by the seminal work of Desiraju on amino-phenol synthon recognition in the solid state. In this event, we cogrinded the SPX zwitterion trihydrate (SPX-ZW-HYD form II), as starting material with 4-hydroxy methyl benzoate (MBZ), -ethyl benzoate (EBZ), -propyl benzoate (PBZ), and -isopropyl benzoate (IBZ) resulted in four cocrystals in a 1:1 stoichiometry and two cocrystal hydrates (SPX-EBZ-HYD and SPX-PBZ-HYD) in a 1:1:3 stoichiometry. In all cocrystals, coformer and drug sustained by amine-phenol synthon and coformer is acting as a proton migrator for the conversion of zwitterion to neutral drug in the cocrystal crystal lattice. All cocrystals exhibited enhanced dissolution profiles compared to the zwitterionic and neutral forms of SPX. All these solid forms were stable at the end of the IDR experiment, as confirmed by PXRD match. This method can be specifically used for oral drug delivery of amphoteric drugs in the neutral form and high solubility (good bioavailability and absorption rate). There are several anti-bacterial, anti-allergic and diuretics as amphoteric drugs, which occur as zwitterions in the solid state with poor membrane permeability. Therefore cocrystallization of these drugs could stabilize the neutral form with improved solubility.