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The Stability of Tamoxifen Introduction Tamoxifen is a well-known medicinal product which was developed in 1960. It is used to treat breast cancer, infertility, bipolar disorder, and gynaecomastia. Its other names are Nolvadex, Istabul and Voladex. It is to be taken orally. 2. Stability of Tamoxifen during Formulation 2. 1. There are two polymorphic forms of Tamoxifen's crystals. The compound that is available normally is found as the meta stable polymorph. When Tamoxifen is crystalized from protic solvents, it starts forming crystals of the stable polymorph which shows disagreeable properties which results in yet additional insolubility of Tamoxifen in water. Thus, it remains stable. These detrimental properties of Tamoxifen influence its absorption performance in vivo which causes a reduction in its bioavailability. Tamoxifen's polymorphic forms prevent the formulation of Tamoxifen Citrate as a suspension thus maintaining its stability during formulation. Because of the low intrinsic solubility of Tamoxifen's molecule, even a little quantity that penetrates the aqueous solution leaves it soon enough, forming crystals of the unwanted polymorphic form. Hence, this level of stability of Tamoxifen during its formulation leads to the necessity of a " liquid formulation of Tamoxifen Citrate where crystallisation will not occur" (Tully 2000). 2. 2. To maintain the stability of Tamoxifen during formulation, the glycol component of the compound should include some (poly) glycol molecules, like polyethylene glycol, of different molecular weights. 2. 3. However, in order to achieve the preferred organoleptic features, it is recommended that the glycol molecules should be of low molecular weight. Glycol which is low in molecular weight may be propylene glycol or glycerol or a mixture of both. 2. 3. If for the sake of stability, propylene glycol is used, then it should be around 10% of the

glycol component by weight. 2. 3. 1. In case, this quantity of glycerol is reduced, then extra measures should be taken to preserve the solution which should be physically stable. 2. 3. 2. Higher quantities of propylene glycol are usually avoided because it has a burning taste. 2. 4. If, for stability, glycerol is used, then it should be around 40% to 50% of the whole glycol component by weight. 2. 4. 1. Although it is not harmful to increase this quantity of glycerol, however the final formulation should not become too thick to process. 2. 4. 2. If this quantity is decreased, then for the relative increase in the quantity of water, it should be noted that the Tamoxifen Citrate would still dissolve considerably. 2. 5. Hence, It is recommended that the glycol component should consist of about 10% by weight of propylene glycol and about 40% to 50% by weight of glycerol, in order to ensure the stability of Tamoxifen. 2. 3. Research also suggests that for the formulation of Tamoxifen at highest stability so that the suspension of a fairly high percentage of Tamoxifen Citrate is made possible and simplicity of processing is maintained, the most favored formulation is a solvent mixture that consists of 15% by weight of ethanol, 10% by weight of propylene glycol, 50% by weight of glycerol, and 20% by weight of a sorbitol solution. The rest is the water. Such a formulation is stable enough to present a physically and chemically stable solution of Tamoxifen Citrate possessing the required amount of absorption. 3. Stability of Tamoxifen till its Release to the Market 3. 1. To ensure the stability of Tamoxifen till its release to the market, the concept of nanoencapsulation has been implemented in the course of its strong ultrasonication and concurrent chronological polyelectrolyte deposition. 3. 1. 1. This is a fresh advancement that changes the thickness of the wall of the capsule so that the drug release rate is

adjusted and an antibody “ at the outer shell layer for targeted delivery” is attached (Ochre Media 2010). 3. 2. Another efficient method is to produce stable nanocolloids of Tamoxifen capsules which should have high substance of the active drug and controllable release rate. For this, a sonicated Layer-by-Layer (LbL) polyelectrolyte coating technology is approached. 3. 2. 1. This approach involves conventional LbL microencapsulation which is based on alternating adsorption of oppositely charged components (linear polyelectrolytes, proteins, and nanoparticles). 3. 2. 2. To attain nanosize cores, aqueous suspensions of Tamoxifen Citrate are made to undergo high potency ultrasonic treatment. 3. 2. 3. Nanopartciles are stabilised in a solution by chronological accumulation of polycations and polyanions and by amassing very thin polyelectrolyte shells over them which have a thickness of 5 to 50 nm and essential composition. 3. 2. 4. After the primary polycation layer is deposited on the nanoparticle, an oppositely charged polyanion is added to it which forms a stable inter-polyelectrolyte complex shell around every drug nanoparticle. The final outermost layer is that of a polymer containing reactive groups like amino groups. It attaches ligands and desirable moieties to the surface of drug nanoparticles. This is how the Tamoxifen is stabilized till its release to the market. References Ochre Media 2010, ‘ Sonication-assisted nanoencapsulation’, Pharma, viewed 21 March, 2011, Tully, RE 2000, ‘ Oral liquid medicine solution’, Patentstorm, viewed 21 March, 2011,