Preparation, *In Vitro* Characterization and *In Vivo* Evaluation of Polymeric Microspheres as a Sustained Release System for Anti-TNF

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**Purpose:** This study aims at the development and preliminary evaluation of polymeric microspheres encapsulating tumor necrosis factor (TNF) inhibitor agent (TuNEX, biosimilar etanercept) as extended release treatment for arthritis.

**Methods:** TuNEX complex was fabricated by using ionic interaction between TuNEX and zinc chloride as drug precursor. TuNEX-poly(lactic-co-glycolic acid) (PLGA) microspheres were prepared via solid/oil/water double emulsion and characterized for drug loading, particle size, surface morphology and *in vitro* release. Pharmacokinetics were assessed in rats after subcutaneous administration. Therapeutic effects were evaluated in collagen induced arthritis model (CIA) in mice.

**Results:** The TuNEX-PLGA MS were successfully developed with drug content of 11.6% w/w and mean particle size of 45.55 μm. The *in vitro* release from PLGA MS formulation followed an initial burst of 35% at 1st day and a continuous release phase up to 35 days. Data from PK study confirmed the prolonged TuNEX exposure for animals treated with TuNEX loaded microspheres and the formulation possessed prolonged *in vivo* pharmacokinetics parameters. We verified the therapeutic effects of TuNEX-PLGA microspheres in the CIA PD model and demonstrated that at same cumulative dose, 5 mg/kg, repeated doses (N=5) showed superior therapeutic efficacy than 25 mg/kg, single dose.

**Conclusions:** A well-controlled release of TuNEX, a water soluble TNF inhibitor, with small initial burst was achieved by utilizing formation of its metal complex forms as a result of possible interaction with PLGA and arginine. These results indicate that the above-mentioned method might be useful for developing sustained-release microsphere formulations in the future.

**References:**