

CHARACTERIZATION OF PLGA-TPGS LOADING PAR-1 ANTAGONIST INHIBITOR TO CONTROL TESTICULAR DAMAGE IN ADULT MALE RATS

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ABSTRACT : The utilization of PLGA-TPGS polymer for nanoparticles to deliver therapeutic drugs as a polymeric matrix performs a high drug encapsulation efficiency. The approval by the FDA of D-Q-tocopheryl polyethylene glycol succinate (Vitamin E TPGS) as a nontoxic pharmaceutical adjuvant, and many TPGS-based drugs delivery system (DDS) have been developed. Our study was achieved to determine the vitamin E - TPGS polymer effects on PLGA loading Zontivity and evaluate stability. Our study reported that Zontivity -NPS, which is destined by the nanoprecipitation method showed that the size of the particle was 185.3 nm of the phase of the nanoparticles. In comparison, high stability was indicated after storage at 191.3 nm. Fifty rats were divided randomly into five equal groups—the first group (T₁): animals' negative control. The second group (T₂): The rats in this group were induced with testicular damage and they were given distilled water as a positive group. The third group (T₃). In this group, the animals had testicular damage and a daily dose of treatment with 1.1mg/kg empty PLGA nanoparticles were given orally. The fourth group (T₄): animals in this group were induced testicular damage and treated with a daily dose of 0.38mg/kg of ordinary Zontivity given orally. The fifth group (T₅): the rats in this group were induced with testicular damage and they were treated with nanoparticles loaded with Zontivity. They were given a daily dose of 0.11mg/kg given orally by stomach tube. Our data showed that Zontivity and PLGA loading, Zontivity, appear to increase viability significantly (P < 0.05) than the positive control group and (T₃) from one side as well as reduce sperm deformity from another side. The histopathological section in the testes of Zontivity loading by PLGA appears semi-normal germinal epithelium, lumen, interstitial tissue and Seminiferous tubules. Thus, improvement of serum level of testosterone was clear that may help to use this new drug to support human fertility in future.

Key words : PLGA, ROS, nanoparticles and seminiferous tubules.

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INTRODUCTION

PLGA are lactic acid and glycolic acid, and complete copolymers. The ratio between the monomers can be varied and often has a big impact on the properties of the copolymer (Makadia and Siegel, 2011). PLGA is approved by the US FDA for different therapeutic applications due to its biodegradability, biocompatibility and sustained-release characteristics (Biondi *et al*, 2008). In recent years, with the coming of block copolymer concept, its utilized as biodegradable, non-toxic and non-immunogenic polymer for the progressing of controlled and targeted drug delivery system has been ultimately elevated (Kapoor *et al*, 2015; Stevanovic and Uskokovic,

2009). Zontivity was the first to market an oral, potent PAR-1 inhibitor and it was recommended for FDA approval on January 15, 2014. It was firstly developed by Schering-Plough before Merck and Co. Took them over and thus obtained the patents (Statkevich *et al*, 2012). The search terms used for Zontivity included SCH 530348, protease-activated receptor-1 antagonist and Zontivit (Hashemzadeh *et al*, 2013). In fact the utilization of PLGA-TPGS polymer for nanoparticles can be as polymeric matrix for therapeutic drugs delivery, in order to perform a high drug encapsulation efficiency, perfect sustained drug release behavior that outcome leads to improved therapeutic efficacy. The object of this study is