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Neuroprotective Equivalence Comparison of Erythropoietin-Ferric/Ferrous Nanobots with Erythropoietin

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ABSTRACT

Erythropoietin (EPO) acts an essential role in neuro-protection and –regeneration in CNS injuries. Their limitations, short therapeutic time window after injury and co-existence of hematopoietic and nonhematopoietic receptors showing phylogenetic and heterogenic differences, can be figured out using quick targeted delivery vehicles such as nanobots. However, EPO has to be released *in-situ* from vehicles in high efficiency as well. To approve therapeutic bioequivalence of EPO-nanobots (ENBs) after breakdown, authors conducted an *in-vitro* comparison study between EPO and ENBs. Nanoparticles (NPs) were manufactured using a chemical co-precipitation method. ENBs consisting of 7.5 mg biodegradable polymer alginate, 1000 IU EPO, and 150 mg ferric-ferrous NPs were synthesized under a nano spray-drying technique. First, as for EPO release rate under control, the ENBs were treated by preconditioning sonication in various degrees (Fig. 1). Second, thapsigargin, endoplasmic reticulum Ca^{2+} ATPase inhibitor, was co-prepared with either EPO only or ENBs. Low frequency preconditioning sonication (from 50 to 60 KHz) up-regulated the accumulative EPO release constantly from ENBs as times went on over 24 hours compared with non-sonication. At early period (2 to 6 or to 12 hours after treatment), each bio-molecular level of JAK2, PDI, PERK, GRP78, AFT6, TGF-β, Casp3, CHOP in ENBs-treated cells was similar to - but significantly different from - that of EPO only-treated cells. However, every marker in ENBs-treated cells reached as the same values as EPO only-treated cells did at 24 hours (Fig. 2 & 3) In conclusion, the ENBs constructed here could display *in-vitro* as the similar level of neuro-regeneration and neuro-protection cascade markers as EPO only did until 24 hours after treatment. In theory, ENBs may make EPO be released under the *in-vivo* control via preconditioned sonication, depending on the degree of sonication. As for a next step of T1 phase, the ENBs will be evaluated under in-vivo physiologic conditions.