10)

عنوان المشروع باللغة العربية - Title of the proposed project in Arabic	تأثير الجسيمات النانوية لأكسيد التيتانيوم على التعبير الجيني لمركب IL-1β, IL-6 and TNF-α mRNAفي أعضاء الجرذان المختلفة
Title of the proposed project in English	Effect of titanium oxide nanoparticles on IL-1β, IL-6 and TNF-α mRNA expression in different organs of rats
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التخصص الدقيق للمشرف الرئيس - Specialty of PI	Biochemistry
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected time in month to finish	12

Abstract of the proposal (No more than 200 words)	Titanium dioxide nanoparticles (TiO2 NPs) are widely used for several applications such as food colorants, drug additives, biomedical ceramics and implanted biomaterials. Several studies have shown immune activation by TiO2 NPs in lungs and heart. Even a low dose of TiO2 NPs can induce long-term adverse cardiovascular effects after oral exposure. An association has been observed between the exposure to TiO2 NPs and the dysregulation of blood brain barrier (BBB) physiology associated with neuroinflammation and decreased expression of neuronal activity, which was further exacerbated in the brain of aged animals inhaled these NPs. Oral intake of anatase TiO2 NPs was found to induce neuroinflammation and could be neurotoxic and hazardous to health. Anticancer therapeutic effects of TiO2 NPs have been linked with oxidative stress and proinflammatory cytokines induction by these NPs. Most of the researches on TiO2 NPs were conducted either in-vitro or they only report local in-vivo effects without highlighting their systemic adverse effects. There is limited data available about the impact of TiO2 NPs on major organs involved in the metabolism and excretion of NPs, and is therefore the purpose of this study.
Hypothesis of the proposal	TiO2 NPs are manufactured in large-scale for various applications, resulting in risks for occupational or accidental exposures of humans. Previous in-vitro studies on cytotoxicity of TiO2 NPs do not necessarily reflect their actual effects in live organisms. A few studies have shown immune activation by TiO2 NPs in localized organs however their systemic effects are poorly understood. It is therefore important to investigate the immunoreactivity of TiO2 NPs for clear understanding of their biocompatibility with particular interest in their biomedical applications. Cytokines are important mediators and regulators of the immune response and are generally recognized as biomarkers of immunotoxicity. Measuring the cytokines gene expression in different organs of rats exposed to TiO2 NPs will provide new insights in the biosafety of TiO2 NPs.
Specific objectives	(1) To determine the proinflammatory cytokines gene expression in different organs of rats exposed to TiO2 NPs. (2) To study correlations among IL-1β, IL-6 and TNF-α gene expressions.
Methodology & Major Techniques to be used	Adult male rats will be randomly divided into treatment groups. One group will serve as control and receive vehicle only. The treatment groups will receive different sizes of TiO2 NPs. The rats in different groups will be sacrificed 24 h and 7 days after the injection of NPs. The specimens of different organs will be

	isolated and immediately immersed in RNA Later solution (Qiagen) and stored at 4°C until RNA extraction. Total RNA will be isolated from different organs using commercial kit (Promega, USA). Expressions of mRNAs for the proinflammatory cytokines, IL-1β, IL-6 and TNF-α will be quantified by real-time RT-PCR. GAPDH will be used as a housekeeping gene for normalizing the expression data. The data were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test using SPSS statistical package. P values less than 0.05 were considered as statistically significant.
Availability of Samples	No
Kindly justify	Samples will be available after animal experiments.
Availability of Chemicals	Yes
Availability of Instruments	Yes
Ethical Approval	In the process
Recent References	1. Khan HA, Ibrahim KE, Khan A, Alrokayan SH, Alhomida AS. Immunostaining of proinflammatory cytokines in renal cortex and medulla of rats exposed to gold nanoparticles. Histol. Histopathol. 2017; 32, 597-607. 2. Khan HA, Ibrahim KE, Khan A, Alrokayan SH, Alhomida AS. Comparative evaluation of immuno-histochemistry and real-time PCR for measuring proinflammatory cytokines gene expression in livers of rats exposed to gold nanoparticles. Exp. Toxicol. Pathol. 2016; 68: 381-390. 3. Khan HA, Abdelhalim MA, Alhomida AS, Al Ayed MS. Effects of gold nanoparticles on proinflammatory cytokines mRNA expression in rat liver and kidney. Biomed Res Int 2013; 2013: 590730.

4. Khan HA, Abdelhalim MA, Alhomida AS, Al Ayed MS. Transient increase in IL-1β, IL-6 and TNF-α genes expression in liver of rats exposed to gold nanoparticles. Genet Mol Res 2013; 12 (4): 5851-5857.
5. Khan HA, Abdelhalim MA, Al Ayed MS, Alhomida AS. Effect of gold nanoparticles on glutathione and malondialdehyde levels in liver, lung and heart of rats. Saudi J Biol Sci 2012; 19: 461-464.