

## RESEARCH HIGHLIGHT

# Prussian blue nanoparticles possess potential anti-inflammatory properties via scavenging reactive oxygen species

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**Iron-based nanomaterials are thought to be cytotoxic in recent researches due to the mechanism that they can produce hydroxyl radical ( $\bullet\text{OH}$ ) in cells via Fenton reaction. However, we found Prussian blue nanoparticles (PBNPs) possess reactive oxygen species (ROS) scavenging ability due to their peroxidase (POD), catalase (CAT), super-oxide dismutase (SOD)-like activities and affinity for  $\bullet\text{OH}$ . We theorized the multienzyme-like activities of PBNPs were caused by their abundant redox potentials in different forms: Prussian White (PW), Prussian blue (PB), Berlin Green (BG) and Prussian Yellow (PY), what makes them admirable electron transporters. The reported PBNPs show anti-inflammation ability in lipopolysaccharide (LPS)-induced cell and animal inflammation models. This Research Highlight discusses the findings of our recent study and related research endeavors.**

**Keywords:** reactive oxygen species; anti-inflammation; peroxidase; catalase; super-oxide dismutase

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Reactive oxygen species (ROS) are highly reactive molecules generated by normal cellular processes, environmental stresses, cigarette smoking, ultraviolet (UV) and  $\gamma$ -ray irradiation. ROS consist of free radicals such as superoxide anion ( $\text{O}_2\bullet^-$ ), hydroxyl radical ( $\bullet\text{OH}$ ) and nonradical species such as hydrogen peroxide ( $\text{H}_2\text{O}_2$ ), which are particularly unstable and will react rapidly with biological macromolecules including proteins, lipids, carbohydrates, DNA and RNA causing cellular and tissue injury. Excess ROS can collapse the ROS generation and neutralization systems in the organism and are thought to be

implicated in many forms of apoptosis and cell death occurring in inflammatory liver injury<sup>[1-4]</sup>, premature aging disorders<sup>[5]</sup>, neurodegenerative diseases<sup>[6]</sup>, cancer<sup>[7]</sup>, diabetes<sup>[8-10]</sup>, atherosclerosis, rheumatic arthritis and heart failure<sup>[11]</sup>. ROS can also activate nuclear factor  $\kappa\text{B}$  (NF- $\kappa\text{B}$ ), enhance transcriptional expression of several inflammatory mediators and finally increase inflammation.

In the field of nano-science, some kinds of synthetic nanoparticles such as platinum nanoparticles<sup>[12]</sup>, vanadia nanowires<sup>[13]</sup> and cerium oxide nanoparticles<sup>[14]</sup> have been

used to inhibit some oxidant-derived diseases because they may mimic one or two kinds of antioxidant enzymes. Generally, iron-based nanomaterials are thought to be cytotoxic in recent researches due to the mechanism that they can produce  $\bullet\text{OH}$  in cells via Fenton reaction<sup>[15]</sup>. The toxicity of iron-based nanomaterials restricts their clinical utility. However, in our recent research, we found that although being a kind of iron-based nanomaterial, Prussian blue nanoparticles (PBNPs) played as an effective ROS scavenger, which acted as  $\bullet\text{OH}$  scavengers and mimetics of three antioxidant enzymes: peroxidase (POD), catalase (CAT) and super-oxide dismutase (SOD). We systematically proved that PBNPs functionally mimic the antioxidants Vitamin C, glutathione (GSH) and N-Acety-L-Cysteine (NAC) via their multienzyme-like activities and  $\bullet\text{OH}$  scavenging ability. The PBNPs could protect cells from oxidative stress induced by many factors, including cisplatin (CDDP), diallyl trisulfide (DATS), UVA irradiation, lipopolysaccharide (LPS), phorbol 12-myristate 13-acetate (PMA), high glucose, oxidized low density lipoprotein (OxLDL) and hypoxic-ischemic. Besides their cytoprotective ability, PBNPs were proved exerting anti-inflammatory effect in LPS-induced animal inflammation models. PBNP pre-treated mice show almost no liver changes after LPS treatment, while untreated mice exhibit symptoms of acute liver disease. ROS levels in liver showed the oxidative stress status was suppressed by PBNPs. Blood biochemical parameters including Alanine transaminase (ALT), serum interleukin (IL)-6 and IL-8 were used to assess the inflammation status. The results show the pre-injection of PBNPs effectively prevents the happening of inflammation. The ROS scavenging ability of PBNPs seems likely to be responsible for their beneficial effects on oxidative stress and inflammation. These findings may shed new light on the mechanisms and applications of nanozymes. Nevertheless, the detailed biological mechanisms still need to be further studied.

### Conflicting interests

The authors have declared that no conflict of interests exist.

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### Author contributions

W.Z. conceived and designed the paper. W.Z., N.G. and Y.Z. wrote and edited the paper.

### Abbreviations

ALT: alanine transaminase; BG: Berlin Green; CAT: catalase; CDDP: cisplatin; DATS: diallyl trisulfide;  $\text{H}_2\text{O}_2$ : hydrogen peroxide; IL: interleukin serum; LPS: lipopolysaccharide;  $\text{O}_2^{\bullet-}$ : superoxide anion;  $\bullet\text{OH}$ : hydroxyl radicals; OxLDL: oxidized low density lipoprotein; PB: Prussian blue; PBNPs, Prussian blue nanoparticles; PMA: phorbol 12-myristate 13-acetate; POD: peroxidase; PW: Prussian White; PY: Prussian Yellow; ROS: reactive oxygen species; SOD: super-oxide dismutase; UV: ultraviolet.

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