IISc team fabricates nanomaterial to treat Parkinson's

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A team of researchers from the Indian Institute of Science (IISc) Bengaluru has fabricated a metal oxide nanomaterial that is capable of mimicking all three major cellular antioxidant enzymes, thereby controlling the level of reactive oxygen species (ROS) inside cells. Based on *in vitro* test results, the nanomaterial appears a promising candidate for therapeutic applications against oxidative stress-induced neurological disorders, particularly Parkinson's. The results were published in the journal *Angewandte Chemie.*

Reactive oxygen species, such as superoxide, hydrogen peroxide and hydroxyl radical, which are generated as part of a normal physiological process, are essential for the normal functioning of cells. Excess of ROS generated is usually controlled by the action of three antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase).

Excess ROS

A problem arises when ROS is generated in excess and the enzymes are unable to control the level of ROS. Oxidative stress due to excessive ROS causes damage to DNA, proteins and lipids; oxidative stress is implicated in several diseases such as neurodegeneration, cancer, diabetes and cardiovascular diseases.

"We have developed a manganese oxide (Mn_3O_4) nanomaterial which functionally mimics all the three antioxidant enzymes. Earlier, we had shown that vanadium oxide (V_2O_5) nanowire is capable of exhibiting glutathione peroxidase enzyme activity," says Prof. Govindasamy Mugesh from the Department of Inorganic and Physical Chemistry, IISc, and one of the corresponding authors of the paper. Nanomaterials with enzymelike activity are called nanozymes. "This is the first time the activity of all three major antioxidant enzymes are seen in a nanomaterial."

The researchers tried several morphologies and found the flower-like morphology had the best activity of all three enzymes. Pores present on the nanomaterial play an important role as enzyme-active sites and help in scavenging excess ROS. The larger pore diameter and pore volume capable of accommodating all the three ROS were found to be critical in determining the enzyme activity of the nanomaterial.

No toxicity

In vitro studies using human neuronal cell lines found that the nanomaterial caused no cellular toxicity when internalised by the cells and hence safe. Metal-based complexes are generally toxic to cells. "The nanomaterial was not toxic probably because manganese is naturally present in our body and is an essential trace element. It is not toxic up to a few microgram. This prompted us to use manganese-based nanomaterial," says Namrata Singh from the Department of Inorganic and Physical Chemistry, IISc and the first author of the paper.

The nanomaterial was found to protect against neurotoxin-induced cell death by scavenging the excess ROS that was artificially generated inside the cells.

"Inside the cells, the nanomaterial was able to substitute the cellular enzymes effectively when the enzymes are inhibited. Due to high pore size and volume, it was able to achieve better activity. So we don't need much of the nanomaterial inside the cells," says Prof. Patrick D'Silva from the

Department of Biochemistry at IISc and the other corresponding author.

Optimum effect

“The manganese oxide nanomaterial was able to control the level of ROS inside the cells. They did not scavenge the ROS completely. If they do then the normal physiological functions of the cells get affected,” says Prof. Mugesh. “It actually scavenges ROS and brings it to optimum level so normal functions of the cell are not affected.”

The superoxide dismutase enzyme has two forms and one functions in the cytosol and the other inside the mitochondria. “Some amount of nanomaterial gets inside the mitochondria as well and controls the ROS produced there. The nanozymes have therapeutic potential particularly for Parkinson’s disease,” says Prof. D’Silva.

Parkinson’s model was tested in the lab. The researchers are trying to design an animal model in mice for in vivo testing.

A study of nearly 300 people living in different parts of India found that nine single-base variants (single-nucleotide polymorphisms or SNPs) account

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