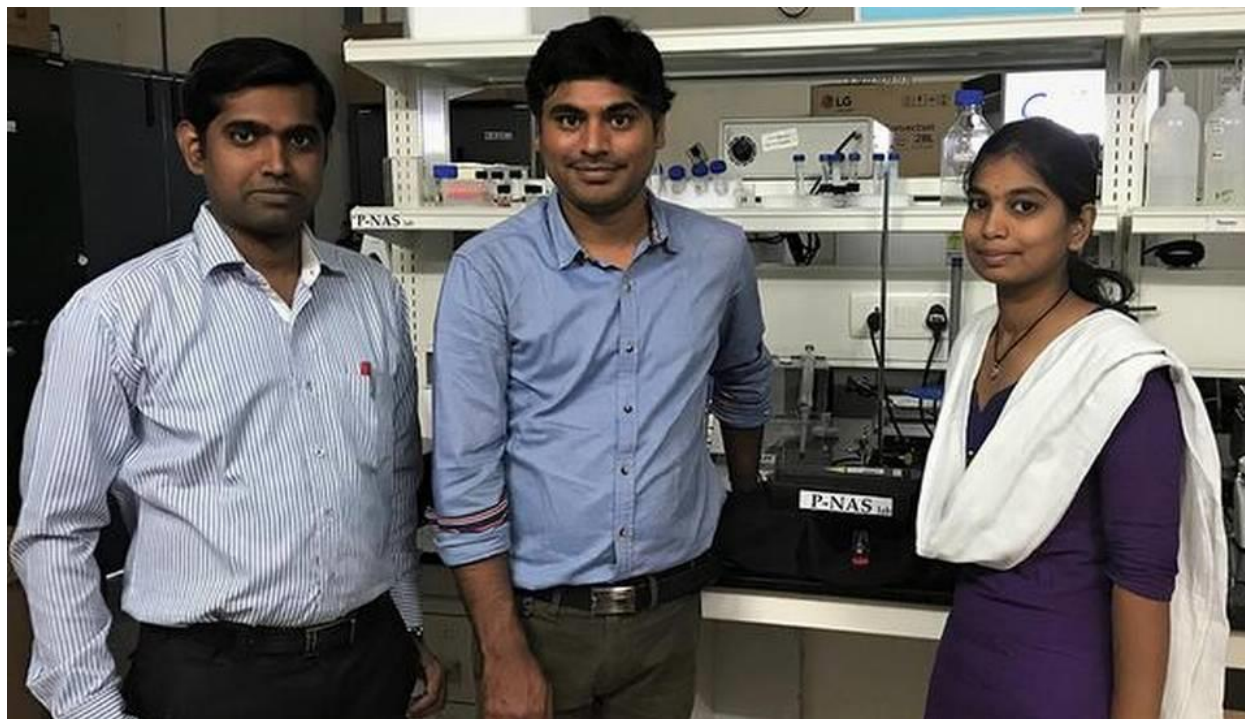


IIT Hyderabad team uses plant extract, heat to kill cancer cells



The nanoparticles, which encapsulate the extract, had no adverse effect on mice, indicating their biocompatibility. Lipid-based nanoparticles encapsulating chlorophyll-rich extract of a medicinal plant *Anthocephalus cadamba* and a near-infrared dye has been found to selectively kill cancer cells when exposed to near-infrared light.

Unlike the conventional photothermal therapy that relies on heat to kill cancerous cells, a multi-institutional team led by researchers from the Indian Institute of Technology (IIT) Hyderabad used heat generated by the dye when exposed to light to destroy the encapsulation and release the extract.

Through in vitro studies, the team led by Aravind Kumar Rengan from the Department of Biomedical Engineering at IIT Hyderabad found that the extract generated excess amount of reactive oxygen species, which caused cell death through autophagy (body's way of removing damaged cells).

Collaborative effort

Researchers from the University of Hyderabad, IIT Bombay and Bose Institute, Kolkata, were part of the study and the results were published in the journal *Nanoscale*.

The extract showed selectivity in killing only cancer cells; the extract released inside normal cells caused insignificant cell death. The reason: the extract did not increase the amount of reactive oxygen species generated inside normal cells thus not causing them through autophagy.

“In our study, heat is used mainly to destabilise the lipid nanoparticle encapsulation and release the extract,” says Prof. Rengan. “We optimised the amount of dye used and the duration of illumination so that the thermal effect is mainly for triggering the release of the extract.”

Potent mechanism

The lethal effect of the extract to kill the cancer cells when exposed to thermal energy was already demonstrated by the team a couple of year ago. But the mechanism through which the extract killed the cancer cells was not known then. “Based on studies using breast cancer cell lines we found that the extract increased the generation of reactive oxygen species, which enhanced autophagy-mediated death of cancer cells,” he says.

When photothermal therapy alone was used, nearly 50% cancer cells died in about 24 hours. But 45% cancer cells grew back in about a day. “But there was no significant growth (about 7.5%) of cancer cells even 48 hours when photothermal therapy was used along with the extract. The extract was able to restrict cancer cell growth,” says Tejaswini Appidi from IIT Hyderabad and one of the first authors of the paper.

Autophagy-mediated cell death was confirmed by using a particular protein that serves as an autophagy marker. “When cancer cells were treated with the extract, the amount of protein marker generated showed an increase. The protein marker produced varied depending on the amount of extract used,” says Deepak Bharadwaj Pemmaraju from IIT Hyderabad and the other first author of the paper.

Reactive oxygen

Since the extract increased the amount of both reactive oxygen species and autophagy, the researchers set out to explore the link between the two. They used a known chemical that inhibits the generation of reactive oxygen species and then treated the cancer cells with the extract. “Cells where the ROS generation is inhibited showed negligible cell death due to reduced autophagy” says Appidi. “This helped confirm the role of reactive oxygen species in causing cell death.”

Similarly, the researchers used an inhibitor to prevent autophagy and treated the cells with the extract. “We saw significant reduction in cell death in the presence of the extract when autophagy was inhibited. This helped confirm the role of autophagy in causing death of cancer cells,” says Pemmaraju. “These two experiments helped confirm that the cell deaths that occurred could be due to ROS-mediated autophagy.”

The efficacy of the nanoparticles containing the plant extract and dye was tested in mouse model with breast cancer. The tumour volume reduced significantly when treated with the extract along with photothermal therapy compared with controls and cells treated with the extract alone. “But the nanoparticles had no adverse effect on the body weight of mice, indicating the biocompatibility of the nanoparticles,” says Pemmaraju.

Source: The Hindu

Date: 21/12/2019