

IIT teams use plant extract, heat to kill skin cancer cells

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Nanoparticle formulation of a chlorophyll-rich biomolecular extract of an Indian medicinal plant *Anthocephalus cadamba* combined with a near-infrared dye has been found to selectively kill skin cancer cells.

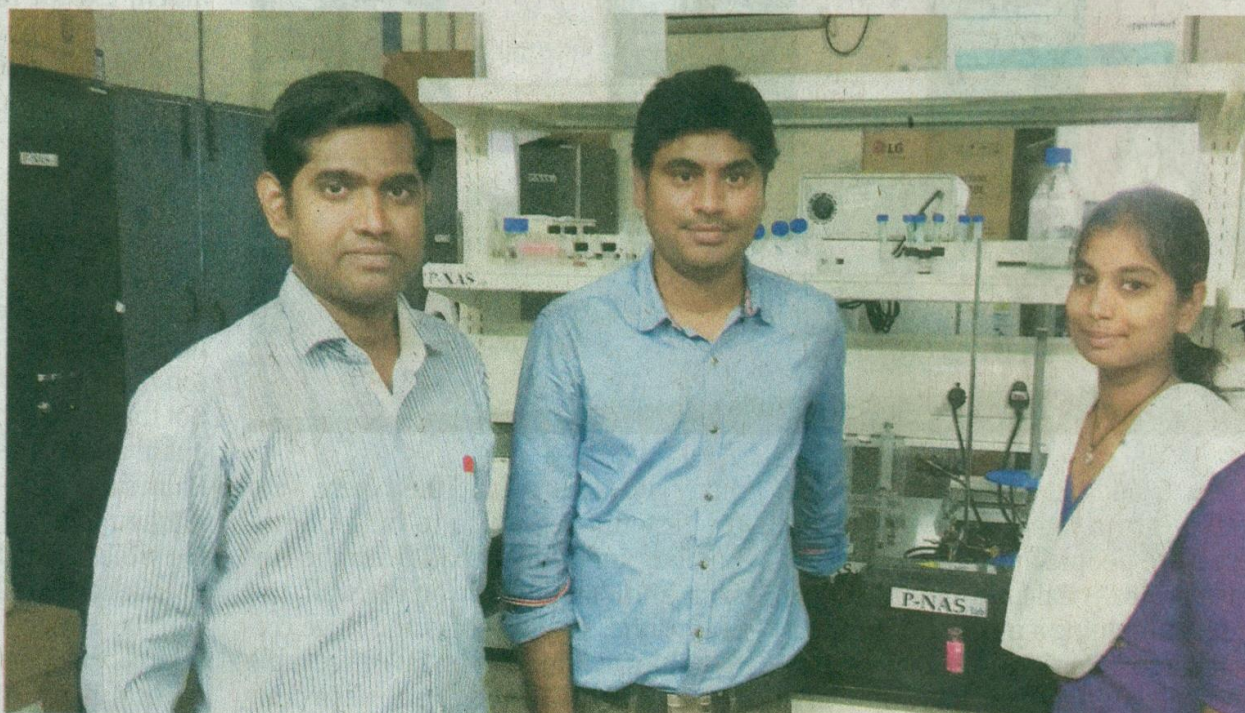
The plant extract is particularly toxic to cancer cells as there is enhanced generation of reactive oxygen species (ROS) while the dye aids in the destruction of cancer cells through photothermal therapy. Near-infrared light was used to heating up the nanoformulation.

The results were published in the *International Journal of Biological Macromolecules*.

Two teams from Indian Institute of Technology (IIT) Hyderabad and IIT Bombay working together have achieved promising results using skin cancer cell lines.

While the plant extract is hydrophobic and hence the uptake by cells will be less, the nanoformulation of the extract makes it less hydrophobic, thereby increasing the bioavailability significantly. The extract and the dye together are encapsulated in a FDA-approved polymer to produce the nanoformulation.

"Uptake of the nanoformulation is nearly the same by normal and cancerous cells. But the extract produces elevated levels of ROS only in cancerous cells. Right now we don't know the precise mechanism by which higher ROS is generated inside cancer cells," says Dr. Aravind Kumar Rengan from the Department of Biomedical Engineering at IIT Hyderabad and one of the corresponding authors of the paper. The levels of ROS inside normal cells were



Discrimination: "Uptake of the nanoformulation is nearly the same by normal and cancerous cells. But the extract produces elevated levels of ROS only in cancer cells," says Dr. Aravind Kumar Rengan (left).

insignificant.

Unlike the highly selective nature of the extract, the photothermal ablation produced by the dye when exposed to near-infrared light is not selective. "So we have minimised the photothermal effect and enhanced the selective toxicity by adding the plant extract. This way, we need to use minimal photothermal effect to kill cancer cells," Dr. Rengan says.

Synergistic effects

"We have been to achieve a synergistic effect by combining the natural extract and photothermal therapy. There was higher cell death when the combination was used than when photothermal therapy alone was used," says Prof. Rohit Srivastava from the Department of Biosciences and Bioengineering at IIT Bombay and the other corresponding author of the paper.

The NIR dye used (IR-780) for photothermal effect is an

inherently imaging agent. The makes the use of any other chemical as an imaging agent redundant.

On being irradiated with near-infrared light, the dye gets heated up and facilitates the release of the extract from polymer membrane. After 4-5 minutes of irradiation, about 80% of cancer cells were killed. After irradiation, the temperature of nanoparticles that contained the dye and the extract increased to 51 degree C. Cells die when heated beyond 42 degree C.

"The nanoformulation with only the plant extract killed less than 20% skin cancer cells while the nanoformulation with only the dye killed 45-50% cells. But the extract and the dye used together killed 82-83% cancer cells," says Tejaswini Appidi from the Department of Biomedical Engineering at IIT Hyderabad and one of the first authors of the paper.

But the crude extract (not

made into nanoformulation) killed 51% cancer cells at 20 microgram per ml concentration. "The reduced toxicity of the extract in nanoformulation was because only very little of the extract could come out of the polymer coating," says Appidi.

"We will be working on different kinds of breast cancer in animal models," says Deepak Pemmaraju from the Department of Biomedical Engineering at IIT Hyderabad and the first author of the paper. "At 780 nm, the penetration of IR will be less than 0.5 cm. The depth of penetration can be increased by using higher IR wavelength."

The use of nanoformulation containing both the extract and the dye will be particularly useful in treating resistant cancer cells.

"The extract that is released will suppress the growth of resistant cancer cells that escape the transient photothermal heat," says Dr. Rengan.

