

Substances from African medicinal plants could help stop tumor growth

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Wild pepper seeds. Credit: Victor Kuete, Institute of Pharmaceutical Sciences and Biochemistry

Experiments using benzophenones derived from plants originating in Cameroon produce evidence that these may be effective against multi-drug resistant cancers.



African medicinal plants contain chemicals that may be able to stop the spread of <u>cancer cells</u>. This is the conclusion of researchers following laboratory experiments conducted at Johannes Gutenberg University Mainz (JGU). The plant materials will now undergo further analysis in order to evaluate their therapeutic potential. "The active <u>substances</u> present in African medicinal plants may be capable of killing off <u>tumor cells</u> that are resistant to more than one drug. They thus represent an excellent starting point for the development of new therapeutic treatments for cancers that do not respond to conventional <u>chemotherapy regimens</u>," explained Professor Thomas Efferth of the Institute of <u>Pharmaceutical Sciences</u> and Biochemistry – Therapeutic Life Sciences at Mainz University. For the past four years, Efferth and biochemist Dr. Victor Keute of the University of Dschang in Cameroon have been studying the active substances in African plants such as the giant globe thistle, wild pepper, speargrass, and Ethiopian pepper.

Multi-drug resistance is one of the most feared problems in cancer therapy because in such cases most of the standard chemical cancer drugs used in therapy fail and the patient's chance of survival is thus dramatically reduced. The problem cannot usually be resolved by simply increasing the dosage as this also results in the exacerbation of undesirable side effects. "We are now looking for substances that can both break down tumor resistance and not produce side effects," continued Efferth, who also works with medicinal plants used in traditional Chinese medicine.

Many plants contain toxic substances that they use to protect themselves against predators and microbial diseases. Over the course of millions of years during which life has evolved on earth plants have managed to appropriate certain molecules to help them to offset their main disadvantage in the face of their enemies, i.e., their immobility and lack of an immune system. The challenge for the pharmacologists is now to determine which plant substances are medicinal and which are simply



poisonous and dangerous.



Sections of the root of the giant globe thistle. Credit: Victor Kuete, Institute of Pharmaceutical Sciences and Biochemistry

During the joint project with Mainz, the Cameroonian scientist Victor Kuete has examined more than 100 spices and plants from his homeland for their cytotoxic effects on cancer cells. Awarded a Humboldt Research Fellowship, he can now continue and extend his investigations as a member of Thomas Efferth's work group in Mainz. "We have already found an entire series of benzophenones and other phytochemicals that are able to elude <u>resistance mechanisms</u> and thus offer many new opportunities for continued research," said Efferth.



The researchers are focusing on three different resistance mechanisms. Transporter-mediated resistance prevents drugs taking effect because a substance called P-glycoprotein promotes their efflux from cancer cells. In the case of tumor-suppressor-gene-mediated resistance, a mutation in protein p53 means that the cancer cells do not die but are resistant and become increasingly aggressive. Lastly, in oncogene-mediated resistance, the epidermal growth factor receptor (EGFR) sends signals into the interior of cells causing tumors to grow faster. The researchers in Mainz have cellular models of all three resistance mechanisms that will enable them to appropriately test the effectiveness of the substances obtained from plants.

In their latest of a total of eight publications produced to date, the research team reports that four naturally occurring benzophenones can prevent the proliferation of the tested cancer cell lines, including multidrug resistant strains. "The benzophenones investigated are potentially cytotoxic substances that need to be more extensively investigated with the aim of developing new <u>cancer drugs</u> that are effective against susceptible and resistant cancers", claims the article recently published in the scientific journal *Phytomedicine*.

More information: Kuete, V. et al. (2013), Cytotoxicity and modes of action of four naturally occurring benzophenones: 2,2_,5,6_-Tetrahydroxybenzophenone, guttiferone E, isogarcinol and isoxanthochymol, *Phytomedicine* 20 (6): 528-536.

DOI:10.1016/j.phymed.2013.02.003

Keule, V. et al. (2011), Anticancer Activities of Six Selected Natural Compounds of Some Cameroonian Medicinal Plants, *PLoS ONE*. DOI:10.1371/journal.pone.0021762



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