Ecstasy derivative targets blood cancers

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PhD student Michael Gandy, who worked on the project and Associate Professor Matthew Piggot. Image: Bob Blucat

(Medical Xpress) -- A team of UWA researchers have found they may be able to alter the club drug 'ecstasy' to kill certain types of blood cancers at the same time boosting the potency and reducing the psychoactivity.

School of Biomedical, Biomolecular and Chemical Sciences Associate Professor Matthew Piggott says when the UWA team was researching the use of Methylenedioxymethamphetamine (MDMA) in Parkinson's disease drug discovery, they came across a paper suggesting it may also be useful in treating blood cancer.

So the UWA scientists collaborated with University of Birmingham Professor John Gordon and his team to increase the toxicity of the drug

toward blood cancer cell lines, while decreasing its psychoactive effects.

While MDMA was never marketed as a therapeutic drug, it was discovered as a 'party drug' in the late
70s and early 80s mainly due to its ability to induce euphoria.

Now, A/Prof Piggott says MDMA's structure can be "tinkered with" with to create MDMA analogues (compounds structurally similar to MDMA) that could have improved therapeutic properties.

"Professor Gordon found MDMA to be weakly toxic to certain types of blood cancer cell lines, so he presented the idea of 'redesigning the designer drug'," he says.

"We contacted him and he was very keen to test our analogues—initially created for Parkinson's disease treatment research—on his cell lines.

"That's how it started."

In order to make the analogues suitable for treatment, the team must focus on removing the psychoactive effect while boosting the toxicity to cancer cells.

To do this, the researchers change some 'substituents', particularly the alpha-substituent, in the analogues, much like removing or adding building blocks. The altered structure modifies the biological properties.

"We had some limited anecdotal evidence...because of the work of maverick chemist Alexander Shulgin, who would make different compounds and test them out on himself and his friends," A/Prof Piggott says.

In terms of increasing its potency against blood cancer cells lines, A/Prof

Piggott says it involves “logical trial and error”.

“Initially six compounds were screened but most were not very active. However, there was one that was ten times more potent, and this became the basis for the next batch of analogues,” he says.

“We are currently at the process of making analogues of the best ‘lead’ compound we have discovered so far—which is 100-fold more potent.”

A/Prof Piggott says the compounds are being evaluated using in vitro cell lines, but the next step would be testing them in an animal model of blood cancer.

Provided by University of Western Australia