System 'prints' precise drug dosages tailored for patients

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Arun Giridhar, an associate research scientist in Purdue's School of Chemical Engineering, works with student Sierra Davis to operate a prototype system to dispense precise medication dosages tailored for specific patients, an advance in personalized medicine that could improve drug effectiveness and reduce adverse reactions. Credit: Steven Yang

(Phys.org) —Researchers have created a prototype system that uses a mathematical model to predict - and a portable inkjet technology to produce - precise medication dosages tailored for specific patients, an

advance in personalized medicine that could improve drug effectiveness and reduce adverse reactions.

Drug makers now manufacture tablets based on clinical studies that determine the average recommended dose. Often this average falls outside of the optimal dose for a particular patient, but there is no way to precisely adjust the dosage except by trial and error.

"Pharmaceutical companies make one or two or three dosage levels, so people try breaking tablets in half and other methods to get to the right dosage," said Gintaras "Rex" Reklaitis, Purdue University's Burton and Kathryn Gedge Distinguished Professor of Chemical Engineering.

Delivering a more precise dosage improves the effectiveness of drugs and reduces potential side effects.

"Many drugs have a minimum effective level, so you need to meet that, and many of them have a toxic level," he said. "The closer you get to it the more side effects there are."

The new approach uses a combination of data and mathematics to determine the precise dosage. Two or three blood samples are drawn from the patient after a small quantity of the drug is administered. Data from those samples are combined with information from clinical studies of larger numbers of patients, and mathematical models are used to determine the proper dose for a particular patient.

Then, a portable technology dissolves or melts the drugs with polymers and uses "drop-on-demand" inkjet printing technology to deposit exact quantities onto tablets or films. Melting medications requires more careful control than simply dissolving them. However, melting could offer benefits over solutions, Reklaitis said. Many of the newest drugs are poorly soluble in the bloodstream. Precisely controlling temperatures

during the melting procedure could allow drug makers to control the drug properties and increase solubility.

"We envision that in its final form the printing will be done in an automated fashion. The pharmacist could key in the dose, the machine prints 20 tablets, and off you go," said Reklaitis, who is working with a team of researchers led by Arun Giridhar, an associate research scientist in the School of Chemical Engineering, and Poching DeLaurentis, a research scientist in Purdue's Oncological Sciences Center.

The team has built a prototype and is working toward commercialization of a device, which is about the size of a large laser printer. Recent research findings are detailed in papers published this year in the Journal of Pharmaceutical Sciences and the journal *Pharmacotherapy*.

The dosage-prediction research was pioneered by Gary E. Blau, a visiting professor in the School of Chemical Engineering, who died earlier this year. It has been funded by the National Science Foundation.

One of the research papers focuses on the mathematical method for predicting a patient's dose while the other describes the drop-on-demand technology applied to solvent-based systems, work that has been supported under the NSF Engineering Research Centers (ERC) program.

"If we say the patient needs 23 milligrams every eight hours, there is no 23-milligram tablet on the market," Giridhar said. "I can make a 23-milligram dose, but to make something that small and that precise is challenging to do with powders. It is much easier to dissolve or melt the drug formulation. Both are viable technologies."

In personalized medicine, physicians use diagnostic methods to determine the precise therapy for each patient.

"We are saying that's great, but you are still faced with the problem of how to administer the drug," said Reklaitis, deputy director of an NSF ERC formed in 2006 to improve the way pharmaceuticals, foods and agricultural products are developed and manufactured.

"In the past, we haven't had the mathematical tools to do this."

DeLaurentis focuses on the mathematical and statistical methods required to determine the drug dosage, building on research initiated by Blau, Reklaitis and former postdoctoral research associate Jose M. Lainez. Giridhar is leading research to develop the portable system with doctoral student Elcin Icten. The work on the printing device also is supported by the Indiana Next Generation Manufacturing Competitiveness Center - IN-MaC - led by Purdue to attract, retain and grow high-value manufacturing industries in the state.

Researchers are involved in clinical studies to learn how effective the procedure is.

The same strategy - using prediction methods coupled with limited blood sampling - could enable health care professionals to monitor a drug's effectiveness over time and adjust the dosage for the patient as needed.

More information: "Dropwise additive manufacturing of pharmaceutical products for solvent-based dosage forms." Hirshfield L, Giridhar A, Taylor LS, Harris MT, Reklaitis GV. *J Pharm Sci*. 2014 Feb;103(2):496-506. DOI: 10.1002/jps.23803 . Epub 2013 Dec 5.

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