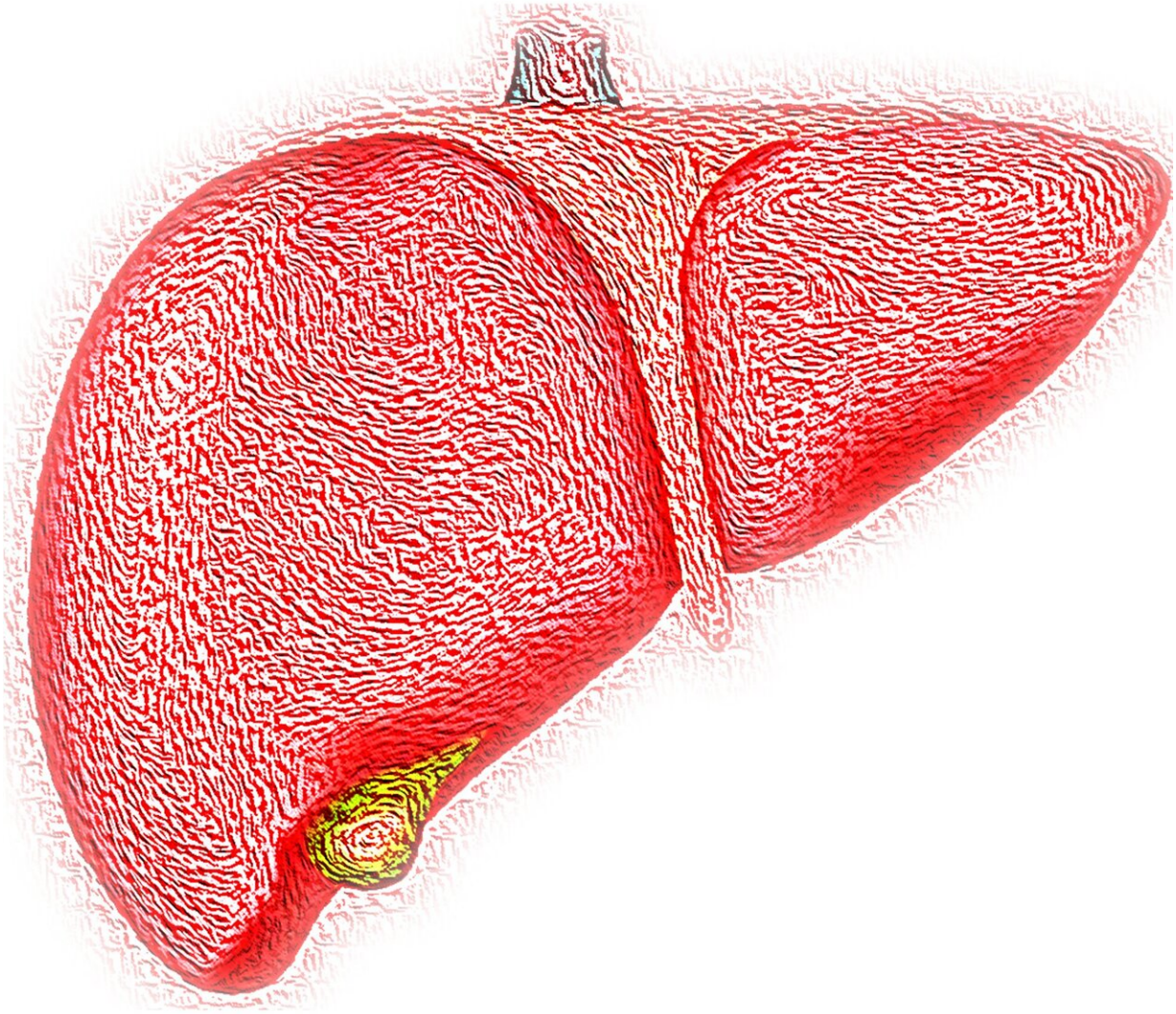
PDMS-based liver-on-a-chip naturally absorbs some drugs, affecting toxicity results

July 28 2021



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Liver-on-a-chip devices capture the physiological and mechanical properties of the liver. They are commonly used by researchers to study how the liver metabolizes different compounds and drugs. In a new study seen in *ACS Biomaterials Science & Engineering*, CiRA Junior Associate Professor Kazuo Takayama and colleagues report which drugs based on their physicochemical properties are most suitable when using liver-on-a-chip technology to study drug toxicity.

One of the most important tests for any drug approval is hepatotoxicity. In fact, the United States Food and Drug Administration claims it is the No. 1 cause of safety-related drug withdrawal from the market. Thus, exhaustive testing is mandatory, as otherwise, a company that has invested billions of dollars on a drug could see it all lost because of this dangerous side effect.

Liver-on-a-chip devices are miniatured models of the liver that include not only liver cells, but also simulate mechanical characteristics of the organ, such as blood flow. The devices themselves are typically made of synthetic material, namely, polydimethylsiloxane (PDMS). PDMS is a silicone elastomer that is colorless and transparent, which simplifies observation of the cells. It is also malleable, making it ideal to mold desired shapes to reproduce the mechanics and fluid dynamics of the liver.

"The problem with PDMS is that it is highly hydrophobic. This means it can absorb drugs, which would affect the results on drug toxicity," says Takayama.

Takayama and colleagues therefore investigated how PDMS-based liver-

on-chip interacts with 12 chemical compounds, including several drugs and their metabolites, in the absence of any liver cells. They found that the partition coefficient, one measure of a drugs' physicochemical properties, was a good predictor of absorption.

They then added liver cells to the liver-on-a-chip to examine how this absorption affected the metabolism of liver cells. Surprisingly, there was no clear correlation between any physicochemical properties, including the partition coefficient, and drug metabolism when the cells were included.

When asked why the partition coefficient would be a predictor in the absence of liver cells but not in the presence, Takayama replied, "It is possible that the hepatic characteristics of the cells changed by the culturing in the PDMS device."

While these results may seem discouraging, they suggest the need for more tools in drug toxicity studies.

"Machine learning the correlation between the drug physicochemical properties and the drug responsiveness of hepatocytes should improve the accuracy of drug toxicity using PDMS-based liver-on-chip," he said.

More information: Sayaka Deguchi et al, Usability of Polydimethylsiloxane-Based Microfluidic Devices in Pharmaceutical Research Using Human Hepatocytes, *ACS Biomaterials Science & Engineering* (2021). DOI: 10.1021/acsbiomaterials.1c00642

Provided by CiRA