Researchers develop high-entropy non-covalent cyclic peptide glass for smart functional materials

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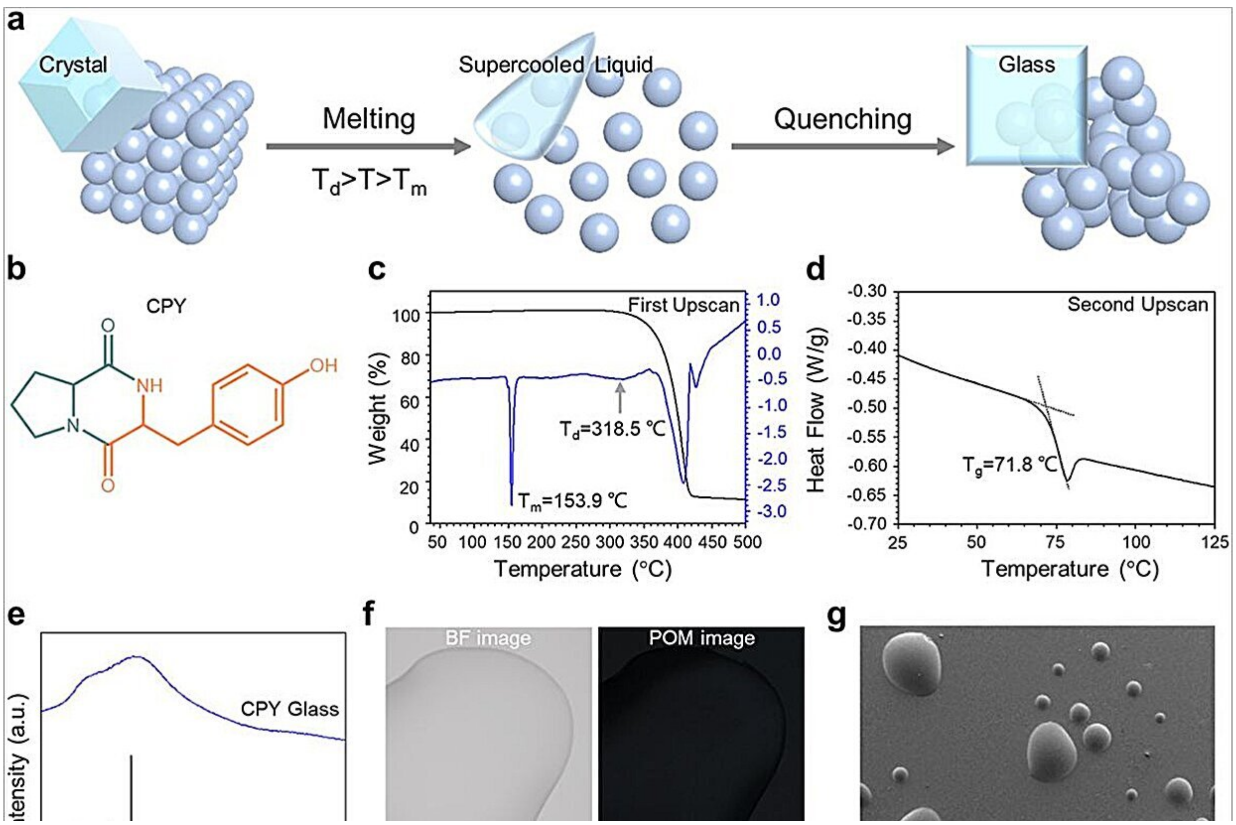

Characterization of CP glass formed using a single component, CPY. Credit: Xuehai Yan

Researchers from the Institute of Process Engineering (IPE) of the

Chinese Academy of Sciences have developed a sustainable, biodegradable, biorecyclable material: high-entropy non-covalent cyclic peptide (HECP) glass. This innovative glass features enhanced crystallization-resistance, improved mechanical properties, and increased enzyme tolerance, laying the foundation for its application in pharmaceutical formulations and smart functional materials.

This study was published in *Nature Nanotechnology* on Aug. 26.

Glass materials have long been integral to technological and cultural advancements due to their versatile properties, such as optical clarity and chemical stability. However, conventional glass materials often rely on strong ionic and covalent bonds, which pose challenges related to toxicity, resource depletion, and environmental persistence. In response, researchers have been striving to develop next-generation glass materials that prioritize biodegradability, biorecyclability, and sustainability.

A research team led by Prof. Yan Xuehai from IPE has pioneered the development of biodegradable, biorecyclable glasses based on amino acid and peptide components. These innovative biomolecular non-covalent glasses offer a sustainable alternative to the traditional glasses and plastics, promising both environmental and ecological benefits. However, developing a stable non-covalent glass that performs well under challenging physiological conditions while minimizing rejection has been a challenge.

Cyclic peptides (CPs), characterized by a cyclic backbone connecting the amino and carboxyl ends, exhibit diverse biological activities, enhanced stability and resistance to enzymatic degradation compared to their linear counterparts. This makes CPs a promising platform for developing non-covalent glass for biomedical or other high-tech applications. However, their strong tendency to crystallize has limited their potential in glass technology.

To overcome this obstacle, the research team developed a novel method to achieve stable non-covalent glass based on CPs. This approach, termed a high-entropy strategy, involved incorporating a diverse range of CPs to create a high-entropy environment that effectively inhibited crystallization.

The CPs underwent a melting-quenching process, where they were heated above their melting points and then rapidly cooled to preserve the disordered conformations in a supercooled liquid state, ultimately leading to the formation of glass. Notably, the principles underlying this strategy are broadly applicable to the preparation of high-entropy non-covalent glass composed of other small organic molecules.

The resulting HECP glass exhibits enhanced crystallization-resistance, improved mechanical properties, and greater enzyme tolerance compared to individual cyclic peptide or linear peptide glasses. These improvements stem from the synergistic effect of sluggish diffusion and hyperconnected network architectures within the HECP glass. Moreover, these properties can be tailored through compositional adjustments, making HECP glass a promising candidate for drug delivery systems where controlled release is essential.

Additionally, HECP glass has already demonstrated the potential to incorporate other functional moieties, such as dyes and nanoparticles, contributing to the design and development of multifunctional, sustainable, non-covalent glasses.

"The high-entropy strategy has proven to be an effective method for achieving stable non-covalent glasses, though it is still confined to laboratory settings at this stage," said Prof. Yan.

Looking ahead, further research is needed to explore the full potential of HECP glass in various applications, including the development of HECP glasses with even higher thermal stability, the incorporation of additional functional groups to enhance their optoelectronic properties, and the exploration of alternative synthesis methods that avoid the use of organic solvents or high temperatures.

More information: Xuehai Yan et al, High-entropy non-covalent cyclic peptide glass, *Nature Nanotechnology* (2024). DOI: 10.1038/s41565-024-01766-3

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