Justification

Currently, the sustainable release of drugs from MOFs have gained considerable. However, three primary approaches have been employed up to this point: i) coating-controlled drug release, ii) drug release regulated by drug-matrix interaction, and iii) drug release initiated by cation.

Majorly synthetic or natural polymeric materials are used in the coating control drug release method to create microparticulate delivery systems. Gelatin is one of the natural polymers that is potentially used in pharmaceutical, biomedical and drug delivery because of its outstanding biocompatible nature, excellent degradability to non-toxic chemicals, and low. Gelatin also increases the biocompatibility of materials. In 2019, Nezhad-Mokhtari *et al.* (*J Drug Deliv Sci Technol* **2019**, *50*, 174–180) performed methotrexate delivery via gelatin-coated Cu-MOF in a very sustainable manner. Similarly, in 2019, Javanbakht *et al.* (*Mater. Sci. Eng. C* **2019**, *96*, 302–309), performed ibuprofen oral delivery via Gelatin coated Cu-MOF in a controlled manner.

In the present work, we have designed/synthesized a new 3D Cu-MOF named **IITI-3** utilized for drug encapsulation by insulin and Hum-insulin. After encapsulation with insulin, it is termed as **insIITI-3**, and further coated with gelatin forms **gel@insIITI-3** to explore controlled drug release.

Owing to the fascinating properties of Cu-MOF, it is widely explored in drug delivery. (*Mater. Today: Proc.* **2022**, *50*, 1906–1911) The prepared Cu-based MOF, **IITI-3, contains high surface area and shows good biocompatibility,** hemocompatibility, and stability. The **IITI-3** showed excellent stability in mammalian cell culture medium (DMEM) in addition to its high stability in a wide range of pH values, a highly desirable characteristic of any compound used as a drug delivery agent. (*Sci. Adv.* **2022**, *8*, eabm4677). The MOFs usually release the insulin faster within 2 to 3 h in stomach acid pH and simulated physiological pH (*J. Am. Chem. Soc.* **2018**, *140*, 5678–5681). The gelatin coating of **ins@IITI3** made it robust for controlled drug release (approx. 4 h). In addition, *in vitro* cellular uptake studies have been performed. The gelatin coating is way more economical than the present-day used coating molecules. Gelatin also enhances biocompatibility/hemocompatibility and is widely used in pharmaceutical industries. (*Mater. Today: Proc.* **2021**, *42*, 240–250, *J Control Release* **2014**, *190*, 210–218, *Biomaterials* **2009**, *30*, 3371–3377, and *ACS Appl. Mater. Interfaces* **2015**, *7*, 18732–18741)

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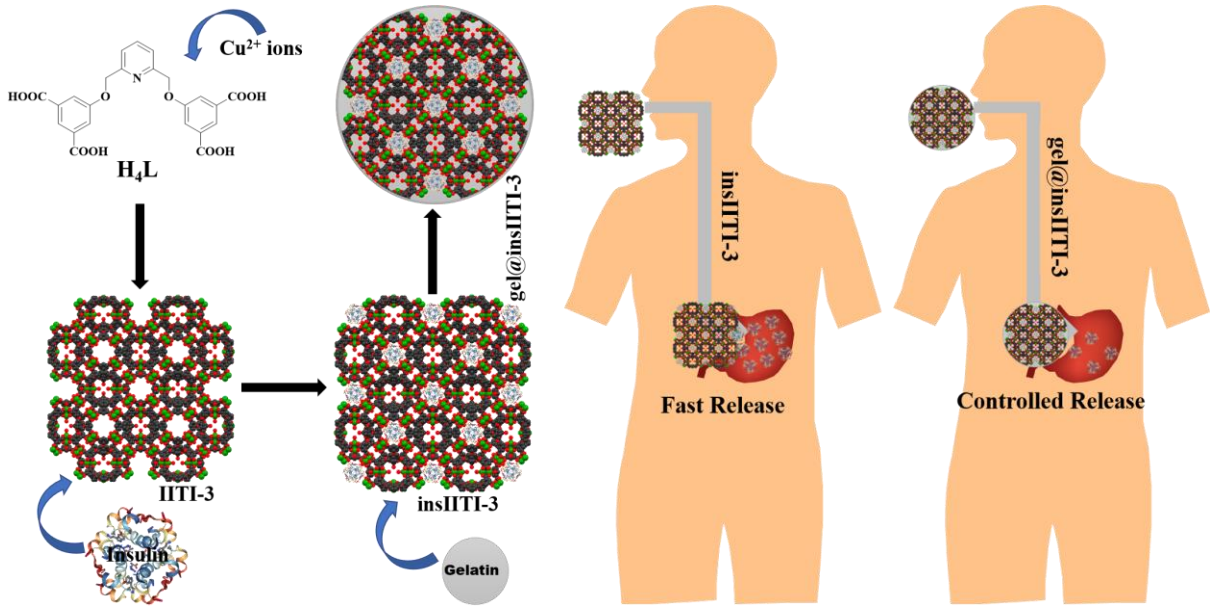

Synthesis of **IITI-3** using new linker, Insulin encapsulation within **IITI-3**, coated with Gelatin and their drug delivery release phenomenon.[1]

Reference:

(1) Kumar, P.; Kaur, N.; Tiwari, P.; Gupta, A. K.; Mobin, S. M. Gelatin-Coated Copper-Based Metal–Organic Framework for Controlled Insulin Delivery: Possibility toward Oral Delivery System. *ACS Materials Lett.* **2023**, *5* (4), 1100–1108. https://doi.org/10.1021/acsmaterialslett.2c01175.

Strongly Recommened

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