BIOMEDICAL MATERIALS

# Luminal coating of the intestine

An orally administered bifunctional gastrointestinal coating has been developed and shown to limit nutrient absorption through the bowel mucosa ultimately lowering blood glucose and also acting as a platform for delivery of drugs to the gastrointestinal tract.

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Incidence of type II diabetes has been on the rise in the past few decades largely driven by low-activity lifestyles and poor diets. It is known that high intake of sugars and fatty foods contribute to obesity and high blood glucose, which are detrimental to health[1]. However, glucose is vital as a source of energy for the survival and normal physiological function of cells, tissues and organs. The gastrointestinal (GI) tract is significantly important for the pathogenesis of diseases such as diabetes and has been widely targeted for the treatment of such complications. Now, writing in *Nature Materials*, Jeffrey Karp, Ali Tavakkoli and colleagues[2] develop a transient coating material that reversibly limits the interaction of nutrients such as glucose with the bowel mucosa and also protects therapeutic agents from exposure to gastric acid and intestinal enzymes.

Currently, a general clinical procedure performed to reduce weight in patients is Roux-en-Y gastric bypass, commonly known as gastric bypass (GBP) surgery. In this procedure, a small pouch is created on the upper region of the stomach and a connection between this pouch and the upper small intestine is made. This leads to reduction in the capacity of food intake and ultimately reduction in the absorption of nutrients, resulting in weight loss. Indeed, GBP surgery is a very efficient strategy for treating obesity[3] and individuals have shown a marked response to it. In patients with type II diabetes, there have been signs of complete reversal of the disease. However, this procedure is associated with a number of complications, such as infections resulting from bacteria in the bowel, hernia and obstruction of the bowel. Moreover, the high financial cost of this procedure also limits its wide use. Other diseases that affect the GI tract could benefit from therapeutics administered orally to target the bowel[4]. However, the efficacy of such therapeutics is limited by the unfavourable environment of the GI tract with regards to its endogenous enzymes and low pH of the gastric acid. To address these challenges, Karp, Tavakkoli and colleagues created a luminal coating for the GI tract that was developed from sucrose octasulfate aluminium complex.

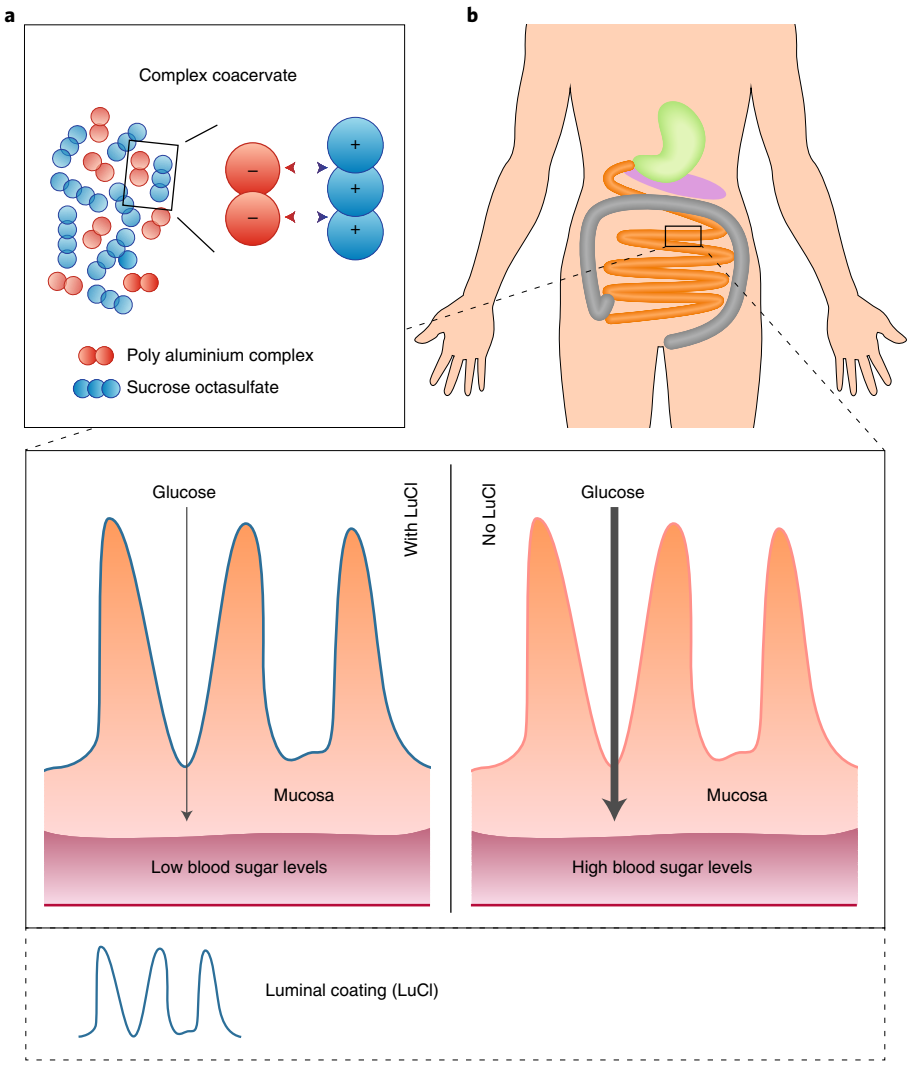


**Fig. 1 | Luminal coating of the intestine to regulate glucose uptake. a**, The coating is developed from complex coacervation of anionic sucrose octasulfate and cationic poly aluminium complex. **b**, When orally administered, LuCl creates a transient and physical coating on the intestinal mucosa. This was investigated in vivo in rats that were subjected to glucose tolerance tests and LuCl was shown to limit glucose absorption and regulates blood glucose levels. Panel **a** reproduced from ref. [2], Macmillan Publishers Ltd.

In an initial screening process, the researchers found that sucralfate outperformed other materials such as methylcellulose and pectin in terms of maintaining a barrier function for hours on a model membrane of mucin-coated porous cellulose nitrate. However, sucralfate

is pH-dependent and only forms a paste in acidic environments and selectively binds to ulcerated mucosa. Indeed, when assessed in vivo, sucralfate only formed sparse aggregates in the stomach and did not have any impact on oral glucose response. Sucralfate has been previously employed in the treatment of ulcers by forming a sticky substance that preferentially binds to the ulcerated regions of the bowel. To maximize bowel coating in a pH-independent manner, the researchers of the current work further engineered sucralfate into a complex coacervate, resulting in the sticky luminal coating (LuCI). Complex coacervation is an electrostatically driven process during which two types of oppositely charged water-soluble polyions form a water-insoluble cluster. For LuCI, these two polyions are anionic sucrose octasulfate and a low-molecular-weight poly aluminium complex, synthesized by acid-mediated hydrolysis of sucralfate (Fig. 1). This irreversible hydrolysis eliminated sucralfates' pH-dependency, creating a paste that may be dehydrated and rehydrated on demand, an important feature for its potential storage as a freeze-dried powder. Compared to sucralfate, LuCI showed similar barrier functions in vitro efficiently blocking glucose diffusion, but independent of pH. In non-diabetic rats, LuCI could significantly reduce oral glucose absorption with the strongest effect observed after one hour and less pronounced after three hours, indicating that the coating is only transiently functional. When rats received LuCI for six consecutive days, no sign of distress or alteration of their bowel architecture were observed, indicating promising short-term biocompatibility. Moreover, there were also no signs of significant weight loss of animals.

The researchers also assessed the potential of LuCI to act as a platform for the delivery of therapeutic agents to the GI tract. Using horseradish peroxide (HRP) in vitro, they demonstrated the ability of the luminal coating to prevent degradation of LuCI to limit damage from simulated stomach fluid and controlled the release of HRP gradually. They also used a model protein, fluorescently tagged albumin, within LuCI and administered it orally in vivo. It was evident that the fluorescent signal could be detected in the stomach and duodenum within an hour of delivery, and in the small intestine within 24 hours, indicating that the protein was not destroyed by the low gastric pH.

The present approach may become a platform technology for other GI dispositions in which ingestion of certain dietary compounds are potentially deleterious. Such applications could include phenylketonuria, induced by absorption of the amino acid phenylalanine from food, and lactose intolerance, triggered by milk lactose. In these diseases, small reduction in absorption of such compounds may substantially improve clinical outcome. Coeliac disease[5] could be another possible target for this therapy. However, it is a more complex case since this severe autoimmune disposition is induced by oral intake of small amounts of dietary wheat proteins (gluten). At the moment, no pharmacological therapy is marketed yet and a strict gluten-free diet remains the only option. In coeliac disease, the autoinflammatory reaction takes place mostly in the upper small intestine. Thus, using LuCI to prevent local absorption of small amounts of gluten in the duodenum could be a promising approach for patients adhering to a gluten-free diet. LuCI may also be combined with exogenous enzymes that are currently being considered for degradation of gluten traces[6]. LuCI could protect these enzymes from GI degradation while simultaneously preventing any uncleaved gluten from systemic absorption.

Overall, this non-invasive avenue for protecting the bowel mucosa from interaction with potentially harmful food components and reducing their systemic absorption is promising. Besides, the authors discuss the possibility to deliver macromolecular drugs to the intestine, which may open numerous applications. Nevertheless, an in vivo delivery approach has only been shown using a relatively simple model protein, albumin, which does not require specific folding. Thus, more complex molecules need to be studied. Further assessment is required to understand how these coatings interfere with normal nutrient and vitamin uptake. Extensive long-term biocompatibility studies will also be needed. Yet, if LuCI in the GI can reduce glucose response under long-term settings and in diabetes patients, it could tremendously enhance their quality of life. ❐

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SPINTRONICS

# Switching by topological insulators

Magnetization in magnetoresistive memory devices can be controlled at room temperature by spin–orbit torques originating from the surface states of topological insulators.

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Magnetoresistive random access memory (MRAM) is a type of non-volatile memory that uses ferromagnetic material to store information at the nanoscale. A contemporary MRAM device typically includes an indispensable component called magnetic tunnel junction (MTJ), which consists of a ferromagnetic/insulator/ferromagnetic (FM/I/FM) sandwich structure. To read the magnetic state of a MTJ, a small sensing voltage is applied across the junction to measure the tunnelling magnetoresistance (TMR). If the magnetizations of two FM layers are parallel to each other (a configuration typically