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Development of dyes/tracers for analysis of renal functions

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Chronic kidney diseases (CKDs) affect a huge population world-wide, where most of these patients do not know they are suffering from a CKD until the later stage. At this point, the treatment options available often lead to poor quality of life without full recovery of the kidney's functioning. The current clinical diagnostic techniques are expensive, cumbersome, invasive and many-a-times not accurate. This creates a need for an early detection way.

Glomerular filtration rate (GFR) is till this date the most used parameter for diagnosing kidney diseases. Nevertheless, tubular secretion and reabsorption play as much a role in healthy functioning of the kidney as does the filtration. The primary focus of this thesis has been to synthesise novel fluorescent markers for evaluating all three physiological processes of the kidneys. This would help diagnosing function-/location-specific abnormality in kidneys. These markers are tested to be used together to evaluate the three kidney functions simultaneously using a transcutaneous device. The detection can be done in parallel with multiple light-emitting diodes (LEDs), or successively. Since the ideal goal would be to measure all the kidney parameters together in a patient, the absorbance and emission wavelength for each marker is designed to be significantly different to evaluate each function distinctly.

The secretion markers have been designed analogous to the known organic anion transporter (OAT) substrates in the blue-green region of the visible light of the electromagnetic spectrum. Fluorescent glucose molecules have been designed as reabsorption markers in the near-infrared (NIR) region. Fluorescently labelled cyclodextrin (ABZWCY-HβCD) was previously designed as a GFR marker in the red-NIR region. All these functional markers altogether pave way for a wholesome, rapid, and non-invasive technique for kidney diagnosis at an early stage.

In addition, fluorescent markers that can assist in kidney imaging were developed, to study its histology using confocal and light sheet microscopy. Fluorescent water-soluble chitosan was developed as a tool for staining kidney vasculature, allowing us to visualise pre- and post-glomerular capillaries along with large blood vessels.

Preliminary results on all the markers show scope for their future biomedical application. Nevertheless, further in vitro and in vivo experiments are needed on the kidney functional markers to confirm their biological activity. Also the use of kidney imaging markers could be extended to other organs. Therefore, follow-up biological experiments are need on other organs, such as heart, lungs, and muscles to test the markers' efficiency.