Does tormentil tincture (*Tormentillae tinctura*) support the therapy of leaky gut syndrome?

The leaky gut syndrome (LGS) is a combination of many disorders in the human body resulting from disturbance of the intestinal barrier's selective permeability. Increased permeability enables penetration of undesirable particles, such as toxins, outside the intestine lumen. These particles can be hazardous to health and may cause symptoms that reduce the quality of life (e. g. flatulence, diarrhoea or constipation, vomiting, chronic fatigue, and headache). The cause of LGS is unknown, but a significant impact of poor diet or lifestyle and infections of enteropathogens is suspected. The existing methods of therapy for the LGS are inefficient and insufficient. Therefore, LGS is a subject over which numerous studies are conducted, and new approaches are sought.

Tormentillae rhizoma (TR) is a traditionally used pharmacopeial plant material with a wide range of applications mainly related to gastrointestinal tract ailments. The herb originates from *Tormentillae erecta* (TE), which is a widespread species in Eurasia. TR is taken orally in a form of decoctions and infusions, but the most popular preparation is a tincture (*Tormentillae tinctura* (TT)).

TR has been used for centuries for the treatment of gastrointestinal tract infections, and its effectiveness has been clinically confirmed. Despite attributed properties and observed bioactivity, the mechanisms responsible for the beneficial effects of TR in gastrointestinal tract ailments have not been yet fully determined. TT as medicine taken orally and with activity related to the gastrointestinal tract, its interaction with gut microbiota should be prioritized while designing studies on its biological properties. Despite the crucial role of intestinal epithelium and microbes residing in its lumen, there are no reports about the mechanism of action of TT and interactions between TT and the human gut environment.

In recent years, the significant contribution of gut microbiota in human organism homeostasis is observed. At first, the microbiota is co-responsible for the intestinal barrier's selective. Moreover, the bacteria present in the gut can convert orally taken compounds which can then be absorbed into the bloodstream and interact with the biochemical processes. After transformations, the final properties of orally applied preparations containing plant materials may differ from the properties of the parental compounds. On the other hand, orally applied therapeutics may alter human gut microbiota's composition, in the positive sense (increasing the gut microbiota diversity) or in a negative (imbalance of the intestinal microbiota). The negative impact on microbiota communities can be observed in LGS applied therapies, which are based on antibiotics and chemotherapeutics, resulting in gut microbiota imbalance leading to significant long-term side effects.

The main aim of the submitted project is to justify the use of tormentil tinctura in the treatment of LGS by verifying the general hypothesis that tannins contained in TT and its gut metabolism products beneficially influence microbiota diversity, inhibit pathogens growth and improve parameters of gastrointestinal barriers.

The studies to confirm the stated hypothesis will be carried out in cooperation between Microbiota Lab (Centre for Preclinical Studies, Medical University of Warsaw) and Institute of Animal Nutrition (Freie Universität Berlin).

The verification of the stated hypothesis will develop the knowledge and give new information about TT compounds' mechanism and their interactions with human gut microbiota and biological activities. It can have great significance in developing effective LGS therapeutic strategies originating from the reintroduction of historically used medicines.