

The number of people with diabetes is constantly increasing, and projections for 2030 indicate 643 million affected individuals. Additionally, one in four people is unaware of their condition, and many patients do not achieve satisfactory results with pharmacotherapy. **Diabetes** is one of the deadliest diseases globally – in 2021, it was responsible for 6.7 million deaths, which means that one person dies every five seconds. Untreated or poorly managed diabetes leads to numerous severe complications. Among these are blood vessel damage that can cause heart disease and strokes, kidney damage (diabetic nephropathy), vision problems (diabetic retinopathy), diabetic neuropathy causing pain and nerve damage, and foot problems that can lead to hard-to-heal wounds and ulcers. More than one-third of diabetes-related deaths occur in people under the age of 60. The World Health Organization (WHO) defines diabetes as a chronic metabolic disease that leads to damage to the heart, nerves, eyes, kidneys, and blood vessels. About 12% of global healthcare expenditures, amounting to 727 billion dollars, are spent on diabetes and its complications, with these costs increasing as the number of patients rises.

One of the most common complications of diabetes is **diabetic retinopathy**, which affects about one-third of patients. Current treatment methods, such as eye drops and ointments, do not provide continuous delivery of active compounds, which is crucial for preventing this disease. The lack of effective therapies in this field results from difficulties in delivering appropriate active substances to the blood vessels in the eye. Diabetic retinopathy is the most common complication of diabetes and the leading cause of blindness, affecting 95% of patients with type 1 diabetes and over 60% with type 2 diabetes. It presents a significant health and socio-economic challenge. **The sudden increase in the number of diabetes and diabetic retinopathy cases highlights the need for early diagnosis and more effective, accessible, and affordable preventive and therapeutic measures.** Research suggests that **polyphenols** – bioactive compounds present in plant foods – may play an important role in reducing oxidative and inflammatory markers in various diseases, including diabetes. Polyphenols have anti-diabetic, antioxidant, and anti-inflammatory properties, making them promising in the prevention and treatment of chronic diseases.

The goal of the project is to develop innovative polyphenol delivery systems to the eyes for effective prevention and treatment of diabetic retinopathy.

The research involves theoretical selection of polyphenols using **molecular docking** to identify those with the greatest therapeutic potential. Then, using **molecular modeling**, auxiliary substances will be selected to support the action of polyphenols. The chosen polyphenols and auxiliary substances will undergo **phase solubility** studies to determine their optimal combinations. The process of preparing polyphenol delivery systems will be optimized using the **Box-Behnken design**, and **dry milling**, an eco-friendly technique, will be used to obtain them. The prepared systems will be evaluated for **solubility** and **dissolution rate** in water and conditions corresponding to the pH of the eye (pH 7.4). They will then be subjected to **stability tests**, including photostability studies and accelerated and long-term studies according to **ICH guidelines**. The physicochemical characterization of polyphenol delivery systems will be conducted using techniques such as **XRPD**, **DSC**, and **FT-IR**. **Biological studies** will include the evaluation of diabetic retinopathy biomarkers (such as VEGF, ICAM-1, TNF- α , PEDF, IGF-1, MCP-1, CRP, TGF- β) using **ELISA kits**. A **polyphenol delivery system-containing ink** will be developed, followed by the design of **contact lenses coated with polyphenol delivery system**. Additionally, a **PLS model** based on FT-IR analysis will be developed to enable non-destructive verification of the polyphenol dose in the contact lenses.

The result of these efforts will be innovative polyphenol delivery systems that can significantly improve the treatment of diabetic retinopathy and other diabetes complications.