Alcohol ranks among the most widely used recreational drugs in the world, even though it is considered a risk factor for more than 200 diseases. The primary negative impact of alcohol lies in its metabolite, acetaldehyde, which, as a highly reactive compound, can form mutagenic adducts and interstrand crosslinks (ICLs) in DNA. The formation of ICLs, which have a covalent nature and block the separation of the two DNA strands during replication, is one of the important causes of mutagenesis and carcinogenesis. To maintain genomic stability, repair mechanisms have evolved. One of them is a pathway that uses proteins encoded by Fanconi anaemia genes, whose defects lead to the disease of the same name. Defects in repair pathways can be particularly dangerous in individuals with impaired functionality in other metabolic pathways, such as alcoholics and individuals with mutations in genes that result in the accumulation of toxic acetaldehyde.

The theoretical part of this thesis deals with alcohol metabolism, *in vivo* acetaldehyde formation, and its interactions with DNA. The ICL and their repair pathways are characterized in more detail. A separate chapter is dedicated to Fanconi anaemia.

The practical part of this work focuses on the preparation of site-specific acetaldehyde-induced ICL (AA-ICLs) and the study of its repair *in vitro*. Specifically, the molecular mechanism of cleavage by the multienzyme complex SLX4-XPF-ERCC1 (SXE), which participates in the FA repair pathway, is investigated. The main outcome of this work was the discovery that upon interaction with AA-ICLs, SXE creates two incisions on the lagging strand of the replication fork, without disrupting the main DNA strand. The first incision occurs at the 5' end of the adjacent strand, followed by cleavage at the 3' end. The obtained results highlight the role of SXE in repairing ICLs during the FA repair pathway, as the unwinding of the ICL-linked parental strands enables the continuation of replication and the restoration of the cell cycle. These findings provide a better understanding of the mechanisms involved in the repair of DNA damaged by ICLs and how cells maintain genomic stability in response to various genotoxic agents.