

I. INTRODUCTION

1.1 Background

Ulcerative colitis (UC) is a disease categorized as inflammatory bowel disease (IBD), which can cause chronic idiopathic inflammation in the mucosa and sub-mucosa of the rectum, extending to the colon (Liu *et al.*, 2021; Yamazaki *et al.*, 2023). This inflammation also initiates the production of oxidative stress, culminating in intestinal mucosal necrosis and ulceration. (Wang *et al.*, 2016). The primary symptoms of ulcerative colitis (UC) encompass diarrhea with a sense of urgency, rectal bleeding, and colicky abdominal discomfort. When UC affects the rectosigmoid region (distal disease), it can manifest with predominant symptoms like rectal irritation, including tenesmus (a feeling of incomplete bowel emptying), small-volume diarrhea, proximal constipation, and rectal bleeding (Ho *et al.*, 2015). A clinical study also demonstrated that patients with UC exhibit an increase in the total white blood cell count, establishing it as a crucial predictor of severe ulcerative colitis (Mack *et al.*, 2020). According to World Health Organization (WHO), the prevalence of UC is estimated to be 200-250 per 100,000 populations (Gupta *et al.*, 2022). Epidemiological studies have shown that the incidence of IBD has an increasing trend in Asia, including Indonesia, Brunei, China, Hongkong, India, Macau, Malaysia, Singapore, Sri Lanka, Taiwan, Thailand, and the Philippines (Park, 2022).

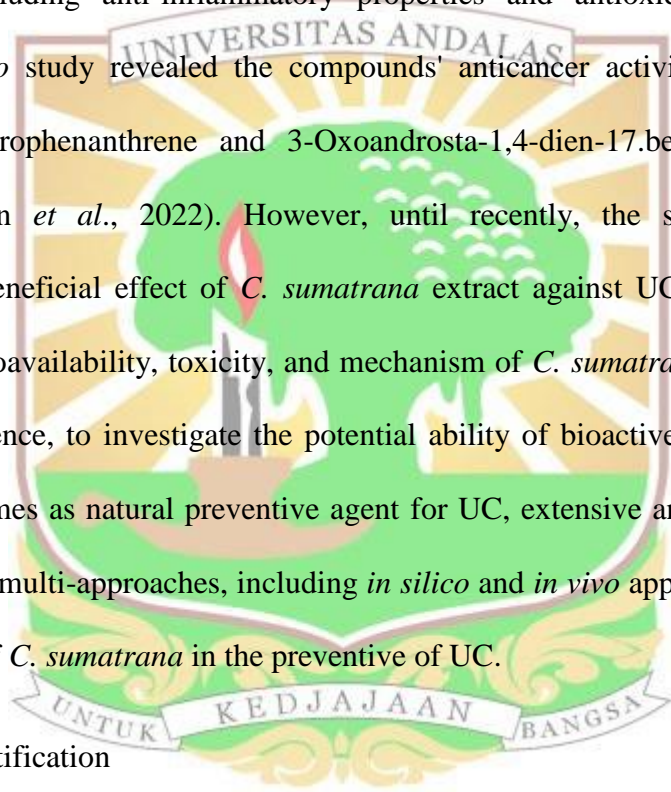
Nowadays, conventional medical treatment offers a broad range of anti-IBD drugs, but some are associated with the risk of adverse effects. For example,

corticosteroids lead to metabolic deregulation, and anti TNF- α antibodies cause skin reactions (Sałaga *et al.*, 2014). An example of another drug, sulfasalazine, causes depression of semen quality and reversible infertility (Ommati *et al.*, 2018). Surgical treatment, such as colectomy, can improve the quality of life in ulcerative colitis (UC) cases with life-threatening complications that do not respond to medical treatment. However, it is essential to note that colectomy carries certain risks, including the potential for colorectal cancer, sexual dysfunction, female infertility, recurrence of inflammation, and psychological disorders (Gupta *et al.*, 2022). Hence, it is crucial to investigate and implement safe and effective approaches to prevent or ameliorate UC.

In recent years, there has been a growing focus on natural products like herbs as potential sources of new drug candidates. Herbs have been utilized for centuries in disease treatment and are perceived as potentially capable of minimizing adverse effects. Natural product-based medicines are gaining popularity and are being adopted worldwide (Choi *et al.*, 2016). Furthermore, medicinal plants and nutraceuticals derived from vegetables have been integral to Asian medicine for over 4,000 years. They have been employed to address various common ailments, including inflammatory diseases (Neto *et al.*, 2016).

Indonesia boasts an extensive biodiversity, which presents promising opportunities for discovering phytopharmaceuticals. It is feasible to explore and transform this biodiversity into potential drug candidates (Laksmiani *et al.*, 2020). *Curcuma sumatrana* is the endemic plant of West Sumatra Province from the

zingiberaceae family (Ardiyani *et al.*, 2011; Wulansari *et al.*, 2020). Previous research on the benefits of *C. sumatrana* conducted by Nawawi (2021), which focused on the advantages of *C. sumatrana*, revealed that the *C. sumatrana* rhizomes composed of 21 bioactive compounds (although only limited to the group of volatile and low molecular weight compounds). Some of these compounds have the potential for various bioactivities, including anti-inflammatory properties and antioxidative stress. Our previous *in silico* study revealed the compounds' anticancer activity, particularly 9-Acetyl-S-octahydrophenanthrene and 3-Oxoandrosta-1,4-dien-17.β.-spiro-2'-3'-oxo-oxetane (Rahman *et al.*, 2022). However, until recently, the scientific evidence supporting the beneficial effect of *C. sumatrana* extract against UC remain deficient. Moreover, the bioavailability, toxicity, and mechanism of *C. sumatrana* extract are also less explored. Hence, to investigate the potential ability of bioactive compounds in *C. sumatrana* rhizomes as natural preventive agent for UC, extensive and in-depth studies are needed using multi-approaches, including *in silico* and *in vivo* approaches, to expand the mechanism of *C. sumatrana* in the preventive of UC.



1.2 Problem Identification

Data on the content of the compounds in the rhizome of wild Sumatra turmeric (*C. sumatrana*) is still minimal, and whether these compounds have a potential for the treatment of ulcerative colitis is unknown. Hence, the major points of this study are:

1. What does the effect of ethanol extract of *C. sumatrana* rhizome on the morphology of the colon (colon length and haemorrhage) in mice induced with piroxicam?
2. What does the effect of ethanolic extract of *C. sumatrana* rhizome on the histopathology of the colon in mice induced with piroxicam?
3. What does the effect of ethanolic extract of *C. sumatrana* rhizome on the quantity of leukocytes in mice induced with piroxicam?
4. What compounds contained in *C. sumatrana* rhizomes act as a potential ligand with a good bioavailability, non-toxic, strong binding affinity, and stable for specific proteins involved in the intervention of the development of ulcerative colitis based on *in silico* approach?

1.3 Purposes of Research

This research explores the potential of chemical compounds in *C. sumatrana* rhizomes as preventive agents of ulcerative colitis through *in silico* and *in vitro* approaches. Specifically, this study aims to:

1. Investigate the impact of the ethanolic extract from *C. sumatrana* rhizome on the morphological aspects of the colon (colon length and hemorrhage) in mice induced with piroxicam.
2. Investigate the impact of the ethanolic extract from *C. sumatrana* rhizome on histopathology of the colon in mice induced with piroxicam.

3. Investigate the impact of the ethanolic extract from *C. sumatrana* rhizome on the quantity of leukocytes in mice induced with piroxicam.
4. Identified the compounds contained in *C. sumatrana* rhizomes act as a potential ligand with a good bioavailability, non-toxic, strong binding affinity, and stable for specific proteins involved in the intervention of the development of ulcerative colitis based on *in silico* approach.

1.4 Benefits of Research

The benefits of this research are as follows:

1. The results of this study are expected to broaden the understanding of the benefits of *C. sumatrana* rhizomes in the prevention of ulcerative colitis
2. The data from this research is expected to serve as a valuable reference for further studies in the natural product-based drug discovery process for ulcerative colitis, mainly using *C. sumatrana* rhizome.

