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Therapeutic role of kaempferol on inflammatory bowel disease through anti-inflammatory effects

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Abstract. Inflammatory Bowel Disease (IBD) is a group of chronic conditions, primarily comprising ulcerative colitis (UC) and Crohn's disease, characterized by inflammation of the intestines. Despite the absence of a specific cause, inheritance, climate, and bacteria disparities are acknowledged to be potential assumptions. Flavonoids, particularly kaempferol, have come to be useful natural remedies for IBD. Kaempferol, a variety of fruits and vegetables, is renowned for its anti-inflammatory, anti-oxidative, and enzyme-modulating components. Kaempferol has been proven to have anti-inflammatory effects through the regulation of inflammatory signaling pathways, including lowering Cyclooxygenase 1 (COX1) and Cyclooxygenase 2 (COX2) levels, regulating Toll-like receptor 4 (TLR4) signaling pathway, and inhibiting pro-inflammation mediators. *In vitro* and *in vivo* models of IBD and UC proved the therapeutic effects of kaempferol through alleviating inflammatory effects, protecting the barrier from dysfunction, and regulating gut microbiota. Further clinical trials are required to understand kaempferol's ability to treat IBD and its potential as a possible pharmaceutical agent.

Keywords: Inflammatory bowel disease, flavonoids, kaempferol, anti-inflammatory effects.

1. Introduction

Inflammatory Bowel Disease (IBD) primarily refers to a group of chronic or recurrent inflammatory conditions of the intestines, primarily ulcerative colitis and Crohn's disease. Although the causeof IBD remains unknown, it is generally accepted that environmental factors, genetic predisposition, and body bacteria's security all play a role [1]. This knowledge has improved both clinical studies and the disease's treatment options. Natural medicines have gained prominence as healthy, alternative therapies for disease issues in recent years. Among them, flavonoids, which are well-known for their anti-inflammatory properties and presence in a variety of foods, fruits, and vegetables, have come into play as potent agents.

Flavonoids are important parts of pharmaceuticals, nutraceuticals, and cosmetics, offering a wide range of health-promoting benefits. Their effectiveness is attributed to their ability to regulate a vital cellular protein and their anti-oxidative, anti-carcinogenic, and anti-inflammatory behavior. Some renowned cases of flavonoids are lipoxygenase, cyclooxyrgenase, phosphatidylinositol 3-kinase, and Antoine oxidase. The well-known flavonoid Kaempferol is frequently used to treat illnesses [2]. Phytochemical like kaempferol have been shown to improve symptoms such as weight loss, stool consistency, and rectal bleeding in IBD individuals. Phytochemicals keep state as a powerful therapeutic option for IBD.

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This review focuses on the potential of kaempferol as a phytochemical agent in improving IBD and its prospects as a future pharmaceutical drug. It will also delve into the chemical structure of flavonoids and explore the pharmacological mechanisms that underlie their effects on IBD.

2. Chemical structure and function of kaempferol

Kaempferol (PubChem CID 5280863) has been found in a lot of fruits and vegetables is kaempferol (3, 5, 7, 7, 7- trihydroxy- 2- (4- hydroxyphenyl- 4H- chromen- 4- one). Figure 1 shows the chemical structure of kaempferol. Additionally, there are numerous other species, like *Magnoliaceae*, *Pinaceae*, *Pteridophyta*, *Aspidistra Eae*, *Polypodiaceae*, and *Albizia Ceae*. Kaempferol, which is a useful tetrahydroxyflavone, has glycolic situations at work 3, 5, 7, and 4. Kaempferol is currently being investigated for its ability as a cancer treatment because of its useful function as an antioxidant and lowering oxidative stress. Additionally, it functions as a human metabolite and xenobiotic agent due to its antibacterial properties [3,4].

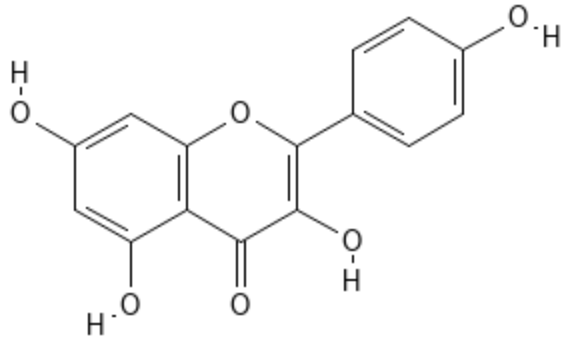


Figure 1. Chemical structure of kaempferol.

3. Kaempferol as one of the active components in plant-based medicine

One of the natural remedies known for its anti-inflammatory properties is the Feather-Leaf Honeysuckle (Crassulaceae), a plant that is used in Brazilian traditional medicine to treat inflammatory conditions. In experimental colitis models, including dinitrobenzene sulfonic acid (DNBS)-induced chest in animals and dextran sodium sulfate (DSS)-induced colitis in animals, it has been hypothesized that the hydroethanolic supply of corn leaf may include anti-inflammatory effects on the bowel system. The presence of flavonoids and kaempferol ingredients as the main flavonoids in these leaf underscores the potency of these factors in addressing gastrointestinal disease [3,5].

4. Anti-inflammatory effects of kaempferol

Reducing problem is regarded as the most potent option in the treatment of ulcerative colitis (UC), and anti-inflammatory treatments are one of the most effective ones. Kaempferol, a typical pectin with known anti-inflammatory properties, has been looked into for possible immunomodulatory effects. In a DSS-induced stomach form, research has examined whether kaempferol may reduce swelling. In feminine C57BL/6J mice, a DSS power group, a bad control group, and several kaempferol post- and post-feeding parties were all included [5]. The results showed that kaempferol significantly reduced the levels of prostaglandin E2 (PGE2) and nitric oxide (NO), both markers of inflammation, in the pre- and post-feeding groups at a dosage of 0.3 %. Additionally, colonic mucosal myeloperoxidase (MPO) activity was inhibited, while leukotriene B4 (LTB4) levels were decreased.

In vivo, kaempferol has been shown to significantly lower Cyclooxygenase 1 (COX1) and Cyclooxygenase 2 (COX2) protein. Arachidonic acid is transformed into pro-inflammatory prostaglandins by the cyclooxyrgenase road produced by physical, chemical, or digital pressure through cyclooxyrgenase substances. Kaempferol essentially stops the inflammatory process by blocking this. When kaempferol is mixed with individual cells and cytokines, COX2 and intracellular nitric oxide (iNOS) costs significantly decrease. The inflammation-related enzyme lipoxygenase (LOX), which

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Kaempferol blocks, is also blocked. Moreover, it reduces nitric oxide, which is linked to pain- related complications and the production of pro-condition cytokines, such as tumor necrosis factor (TNF)-α [5].

Kaempferol, a function sign for colon phlegm tissue, was more prevalent in post-fed creatures. These analyses demonstrate that the colonic mucosa is protected from DSS-induced UC by kaempferol's potency as an anti-inflammatory broker. Additionally, the results demonstrated that kaempferol's ability to inhibit some colitis-related signs was enhanced by stomach training.

Utilizing lipopolysaccharide (LPS)-induced rat intestinal microvascular endothelial cells (RIMVECs), further studies examined the effects of kaempferol on intestinal inflammation. In addition to intercellular adhesion molecules 1 (ICAM-1) and vascular cell adhesion molecules 1 (VCAM-1), a kaempferol pretreatment reduced the production of pro-inflammatory cytokines like TNF, IL-1, and IL-6. These cuts suggest that the weak TLR4, NF-B, and STAT signaling pathways does contribute to kaempferol's anti-inflammatory effects. These studies generally demonstrate the potency of kaempferol in addressing IBD [6].

5. Applications of Kaempferol in IBD

Kaempferol, a nicely- known flavonoids, has attracted interest for its potentiating function as a cure for IBD and its anti- inflammatory properties. An effective immune response causes chronic inflammation of the gastrointestinal tract, which includes Crohn's disease and ulcerative colitis. The condition also results in diarrhea, throat pain, and vaginal bleeding because it drastically impairs the colon surface. Typical treatments, such as immunosuppressants and treatment, are frequently successful, but prolonged usage frequently results in negative results and challenges. Kaempferol is a promising choice or other to managing IBD because of its natural source and multi-targeted mechanism of action. Table 1 summarizes current research on the the therapeutic effect of kaempferol in IBD.

5.1. Reducing pro-inflammatory signaling

One of the main ways that kaempferol prevents IBD is by reducing the levels of pro-inflammatory cytokines, which are enzymes that cause immune cells to initiate an aggressive response. Using animal models of colitis, which are similar to human IBD, studies have found that kaempferol significantly lowers the levels of interleukin-1 β (IL-1 β), interleukin-6 (IL-6), and other hormones that are elevated during intestinal inflammation. These cytokines never only make the angry system worse, but they also exacerbate the situation by destroying the intestinal organs. Kaempferol encourages cure by smashing this time by preventing the production of these cytokines [7].

Kaempferol's ability to regulate the Toll-like receptor 4 (TLR4) signaling pathway is another important component of its IBD action. One of the key elements of the body's inherent immune system's ability to recognize fungal fragments is TLR4. Because of TLR4 route activation, IBD triggers sporadic protection responses and prolonged swelling. In response to lessening infection and the immune response, kaempferol has been shown to lower TLR4. Kaempferol is a promising candidate for extended- word use in IBD treatment because it reduces swelling without reducing total immune function due to its ability to change defensive system action without absolutely suppressing it.

The benefits of Kaempferol are beyond affecting the immune system. The oxidative stress that prevents IBD from heading is prevented by its antioxidant qualities. Inflammation is frequently brought on by reactive oxygen species (ROS) overproduction. To shield the tissue in the colon concealing from oxidative damage, Kaempferol harvests these free radicals. This antioxidant action reduces swelling and aids in preventing the long-term effects of chronic oxidative stress, such as the increase in IBD patients ' risk of developing colorectal cancer.

5.2. Alleviating symptoms

Kaempferol has been shown to have a renowned ability to reduce IBD symptoms in experimental studies. For instance, a study using mice with dextrose sodium sulfate (DSS)-induced colon, a condition that frequently mimics human chronic diarrhea, found that a kaempferol treatment significantly improved several scientific indicators of diarrhea. A slimmer office, fewer uterine hemorrhage, and lessening large

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were just a few of the improvements [7]. Additionally, it was discovered that immune cells cannot provide the colonic mucosa, which is a sign of strong diseases, without the aid of kaempferol. These analyses demonstrate that kaempferol addresses the condition's underlying creates while lowering the severity of the condition.

The intestinal barrier function, which IBD people typically struggle with, has been shown to be protected by kaempferol. By blocking the passage of dangerous substances into the mind, such as microorganisms and waste, the intestinal barrier is crucial to maintaining gut health. This issue weakens IBD by increasing intestinal intake, which is frequently referred to as "leaky gut." As more dangerous substances enter the body's immune system, this problem worsens the aggressive answer. According to research, kaempferol increases the appearance of tight junction proteins, which are crucial for maintaining the dignity of the stomach challenge. By reducing this problem, Kaempferol breaks the IBD's violent period of illness and obstacle function [8].

Despite the fact that the majority of research was done using *in vitro* and *in vivo* models, kaempferol has a significant possibility for use in medicine in patients. Kaempferol might change or get a workable substitute for conventional IBD medications as more clinical trials are conducted. It is a multifaceted healing agent with fewer side effects than conventional remedies because of its ability to alter security systems, reduce oxidative stress, and protect the intestinal barrier.

Table 1. Applications of kaempferol in IBD

Models	Treatment methods	Results	Ref(s)
Female C57BL/6J mice with DSS-induced colitis	0.1% or 0.3% kaempferol	Kaemferol protected colonic mucosa	[5]
Epithelial-endothelial cells co-culture model	80 μM kaempferol	Kaempferol significantly lowered the inflammation, and alleviated barrier dysfunction, through inhibiting NF-κB signaling pathway	[7]
Female C57BL/6J mice with DSS-induced colitis	14 days of kaempferol (50 mg/kg/day), gavage	Kaempferol decreased serum LPS and TLR4-NF-κB signaling, and regulated gut microbiota. Kaempferol alleviated ulcerative colitis (UC).	[8]

Abbreviations: IBD, Inflammatory Bowel Disease; DSS, dextran sulfate sodium; TLR4, Toll-like receptor 4; NF-κB, nuclear factor kappa beta; UC, ulcerative colitis.

6. Conclusion

In conclusion, due to its anti-inflammatory and anti-oxidative properties, kaempferol, a naturally occurring flavonoid, has a significant potential to treat inflammatory bowel disease (IBD). By inhibiting proteins such as COX1, COX2, and lipoxygenase, Kaempferol reduces bowel disease by decreasing the production of pro-inflammatory cytokines, including TNF and nitric oxide. Kaempferol protects colonic mucosa and lessens ulcerative colitis symptoms, according to studies using both *in vitro* and *in vivo* models. Furthermore, kaempferol regulates inflammatory signaling, such as TLR4 and NF-κB, supporting its role on IBD. Kaempferol's mechanisms of action need to be more extensively studied in women's clinical trials as research improvements to realize its efficacy and safety. As part of a comprehensive treatment plan for IBD and other inflammatory disorders, coming research should also include the development of kaempferol-based medications and nutraceuticals.

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