CASE STUDY: **Effects of Enzyme Therapy on Ulcerative Colitis**

ABSTRACT

Although the medical treatment of ulcerative colitis (UC) has advanced significantly in recent years, with the introduction of novel small molecules targeting multiple immune effectors, and with more new options to come, a cure for this at times devastating disease is not on the horizon. Most drug development efforts currently focus on blocking the inflammatory cascade, which most likely is, at least in part, a secondary rather than a primary event. The initial pathogenic level of UC appears to be the slow invasion of commensal bacteria from the colon lumen into the mucosa, facilitated by a mucus barrier dysfunction (leaky gut). Much like in Crohn's disease, the immune response in UC is directed against bacterial antigens, leading to a predominantly mucosal inflammation beginning in the rectum and variably migrating orally to the cecum. Enzyme therapy has been reported to decrease inflammation and support intestinal barrier function and proper digestion. Proteolytic enzymes having anti-inflammatory properties along with other digestive enzymes, herbs, and probiotics that ensure optimum digestion and absorption of nutrients as well as facilitating removal of waste may be a novel therapy for addressing root cause of inflammatory bowel disease (IBD) including UC. The purpose of this case study was to determine if Transformation Enzyme Corporation's Leaky Gut Protocol combined with high dose protease could be tolerated and work as a more natural and safer alternative to traditional treatments for a patient with UC. The participant of the current case study was placed on this protocol for approximately 6.5 months to evaluate the effectiveness of enzymes and probiotics on this condition. The objective is to observe healing of the ulceration, decrease GI inflammation, improve bowel movements from constant bloody diarrhea to normal fecal matter, decrease pain, and improve tolerance to a variety of foods.

INTRODUCTION

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), is a global disease with the highest incidence in Western countries, although the incidence is increasing in newly industrialized countries. UC is a relapsing and remitting inflammatory bowel disease characterized by mucosal inflammation which starts distally and can extend proximally to involve the whole colon. UC presents with bloody diarrhea, frequency, abdominal pain, fatigue, and fecal incontinence. The etiology involves interactions between the environment, immune system, gut microbiome and a genetic predisposition to disease. It has been suggested that environmental factors play a major role in the pathogenesis of IBD. Early life events such as mode of birth, breastfeeding, and exposure to antibiotics and other factors such as air pollution, smoking,

psychological state, exercise, and diet are among the potential environmental contributors of IBD development or disease activity. Significant changes in dietary intake during the past decades have also been associated with the increase in incidence of UC. The relationship between diet and UC development has been indicated in several epidemiological studies. Although the exact mechanisms responsible for the association between diet and development of inflammatory bowel disease is unknown, several mechanisms have been suggested.

An unhealthy dietary pattern such as a Western diet has been linked to changes in the gut microbiome and epithelial barrier function and seems to have a direct influence on immune function, triggering a pro-inflammatory environment characterized by an imbalance in the T helper 17 (TH17) cell to regulatory T (Treg) cell ratio. The intestinal mucosal barrier, which consists of intestinal epithelial cells and intercellular tight junctions, plays a significant role in maintaining intestinal homeostasis and resisting intestinal infection. A breached intestinal barrier allows microbes unlimited access to the lamina propria and the bloodstream, a condition referred to as “leaky gut.” IBD patients often suffer from abnormal intestinal permeability and enteric blood barrier impairment. Thus, studying the interactions between the gut microbiota, gut immunity, enteric nervous system, and the intestinal barrier may help further understand the pathogenesis of IBD and provide options for future treatment.

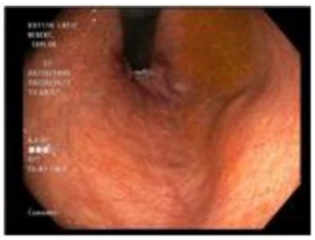
Conventional treatment for ulcerative colitis includes anti-inflammatory medications, steroids, immune system suppression medications, and biological therapies. These medications generally work by blocking the inflammation in the body in various ways and putting the inflammation into "remission." Most drug development efforts currently focus on blocking the inflammatory cascade, which most likely is, at least in part, a secondary rather than a primary event. While these medications can provide symptom relief, they do not address root cause and can be accompanied with unwanted side effects. The successful initiation of an immune response depends on T cells and macrophages, along with the polypeptide factors they produce, called cytokines, which play a key role in communication during normal immunological response as well as infectious, inflammatory, and neoplastic disease states. Supplemental enzymes have all been demonstrated to induce cytokine production in human peripheral blood mononuclear cells. Treatment with these enzymes leads to the production of TNF-alpha, IL-1 beta, and IL-6 in a time and dose dependent manner. Proteases such as Papain and bromelain have a 10- to 40-fold inducing capacity for TNF production. Macrophage activity is enhanced up to 700% and phagocytosis is also accelerated with the induction of systemic enzyme therapy. Proteolytically active enzymes such as bromelain are known to decrease expression of mRNAs encoding proinflammatory cytokines by human leukocytes in vitro. Significant increases in these proinflammatory cytokines such as granulocyte colony stimulating factor (G-CSF), interferon (IFN)-γ, interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF) are detected in the media from actively inflamed areas in various disease states.

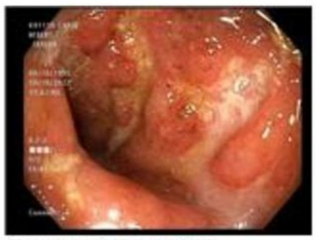
Due to the role diet, inflammation, and intestinal health play in the development of this disease, a program that addresses diet and lifestyle and provides gastrointestinal support is essential for those suffering from this condition. Disease does not happen overnight. It takes years of this constant neglect and over-indulgence to alter our enzyme balance and create a disease condition. Transformation Enzyme Corporation's Thrive in 63 program is the result of our “leaky gut” study completed in September 2014. This evidence-based clinical review showed that if patients are given specific guidelines on what to eat and support those dietary modifications with a simple and effective enzyme protocol, we not only eliminate many symptoms but also begin healing the root of the illness—the gut—in as little as 2 months. The rationale behind the program is simple: give the body the nutrients it needs, clear away the waste, and allow the body to manage its resources. For a minimum of 21 days, all patients begin on Transformation’s gentle formulations. These are well-tolerated by the majority of patients and an ideal starting place for individuals who may be sensitive to supplementation or dealing with inflammatory conditions such as UC. After the initial 21 days, patients can progress to the more therapeutic formulations for the remainder of the program if tolerating well.

CASE STUDY

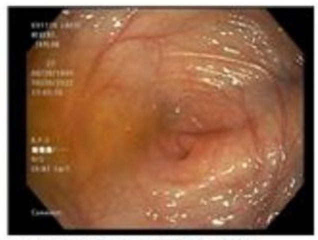
In this present case study, we have a 28-year-old female patient with severe UC which began in November 2020 and was confirmed via colonoscopy in October 2022. The patient complained of blood and mucus in the stool which occurred 15 or more times a day and noticed that fasting / bland diet seemed to slightly help. She experienced frequency / urgency of bowel movements and diarrhea accompanied by sharp abdominal left lower pain daily. She also experienced hair loss which began in February 2021 and took folic acid and iron supplements that seemed to help. Other symptoms she lived with were achy joints, anxiety, GERD, bloating, depression, anemia, eczema, chronic fatigue, shortness of breath, headaches, poor concentration, and brain fog, just to name a few. She had been taking Vyvanse® for 8 years for ADHD, Xyzal® for 8 years for allergies, Omeprazole for 2 years for GERD, and Ogestrel for 2 years for irregular menses. Her ability to eat a variety of foods without experiencing acute symptoms was very limited, and despite this limitation she was unable to lose weight and weighed 165 lbs.

Initial Colonoscopy, 10/20/2022:

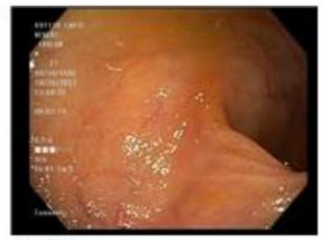




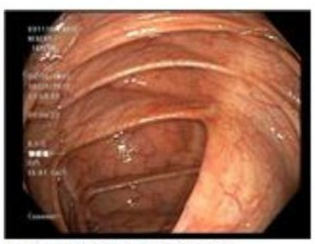
Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



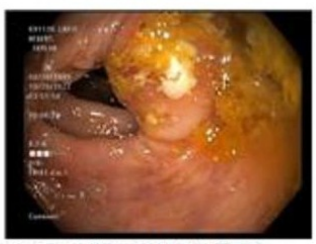
appendiceal orifice cecum normal



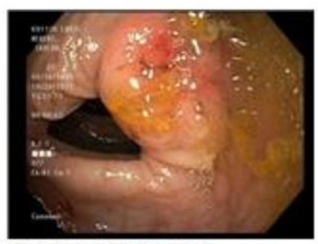
normal



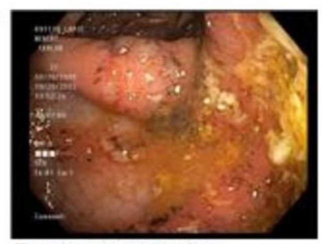
ascending colon normal transverse colon



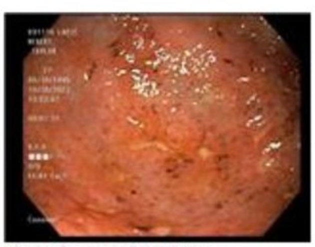
descending colon at 50 cm where the inflammation is starting



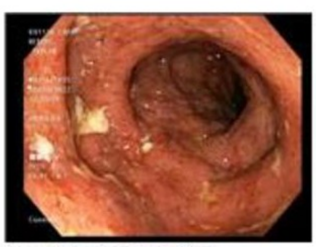
Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



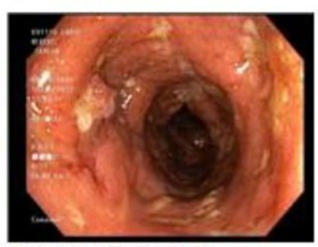
Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



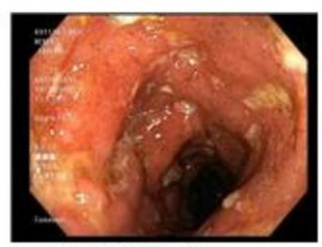
Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum



Erosions, congestion, granularity, ulceration and aphthous ulceration in the descending colon, sigmoid colon and rectum

On this first colonoscopy above, before any intervention with the enzyme protocol, they found in the mucosa diffuse continuous erosions, congestion, granularity, ulceration, and aphthous ulceration with spontaneous bleeding noted in the descending colon, sigmoid colon, and rectum. There was no inflammation in the ascending, transverse, and proximal descending colon. Starting at 50 cm from the anal verge the patient had severe inflammation in the colon that was continuous and circumferential. She did have some deep ulceration in some of the regions of inflammation. In the rectal region she had mild inflammation.

October 2, 2023: We began Phase 1 of Transformation Enzyme Corporation's Thrive in 63 protocol which consists of Transformation's sensitive digestive, anti-inflammatory, and probiotic formulations. The patient began with 3 capsules of DigestZyme and 1 capsule of PureZyme before each meal, 3 capsules of GastroZyme after each meal, and 3 capsules of Plantadophilus along with 3 additional capsules of PureZyme at bedtime. Due to the level of inflammation suspected based on clinical history and symptoms, it was determined that starting with the sensitive line of digestive, gut lining, and inflammatory support would be best.

October 30, 2023: The patient was tolerating Phase 1 well so we substituted PureZyme and GastroZyme with the more potent Transformation Professional Protocol™ formulas as follows: 1 capsule of Protease and 1 capsule of Gastro, respectively, at the same dosing times as well substituting as the PureZyme at bedtime with the Professional Protocol™ Protease.

November 3, 2023: We next substituted DigestZyme with the more potent Professional Protocol™ Digest formula. The patient's protocol was now 1 capsule of Digest and 1 capsule of Protease before each meal, 1 capsule of Gastro after each meal, and 3 capsules of Plantadophilus along with and 2 capsules of Protease at bedtime.

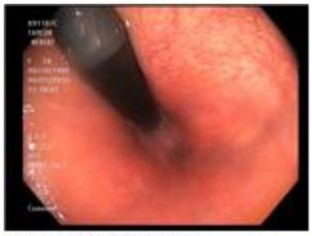
December 5, 2023: We then substituted the Plantadophilus with the more potent Professional Protocol™ Probiotic formula, from 3 capsules of Plantadophilus to 1 capsule Probiotic at bedtime, with the rest of the dosing schedule remaining the same.

January 9, 2024: The patient discontinued the Omeprazole for the first time in 2 years and discontinued and the Ogestrel® for the first time after 8 years.

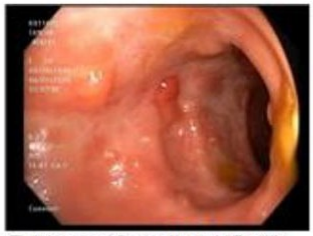
January 11, 2024: We increased the supplementation protocol again by adding probiotics in the morning, proteases between meals, and an additional capsule of digestive support between meals. The dosage schedule was now 1 capsule of Probiotic morning and night, 1 capsule of Digest before each meal, 2 capsules of Gastro after each meal, and 2 capsules of Protease three times daily on an empty stomach.

February 25, 2024: We increased the enzyme therapy even more by substituting the Protease capsules with 5 grams of powdered Protease 3 times daily due to the need for extensive inflammatory support. We wanted to observe clinical changes with "mega" dosing along with tolerance of someone with this condition who typically may not be able to tolerate a systemic formula of this magnitude at that dose. The patient continued with the digestive enzymes with each meal and the probiotics in the morning and night. The patient was given a followup colonoscopy April 1st to note any difference in clinical findings, and the supplementation protocol was followed until April 20th when we concluded the study.

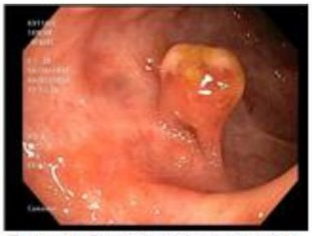
Followup Colonoscopy, 4/1/2024:



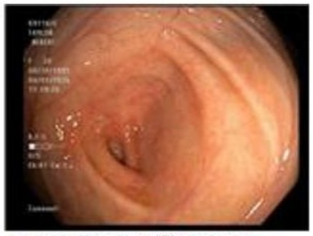
Internal hemorrhoids



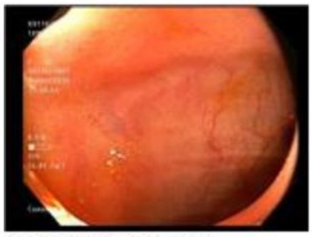
Evidence of previous UC with areas of burned-out Nissen pseudopolyp starting roughly in the sigmoid region/descending colon



Polyp (12 mm to 14 mm) in the sigmoid colon

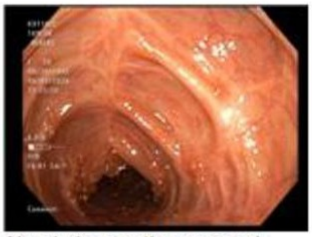


appendiceal orifice cecum normal

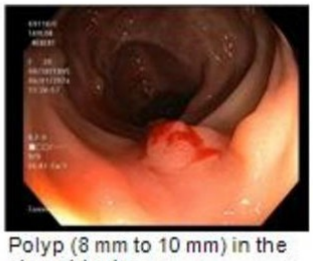


terminal ileum normal

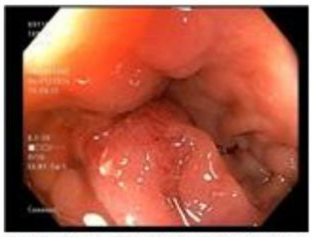
Fair bit of pseudopolyps starting in the descending colon



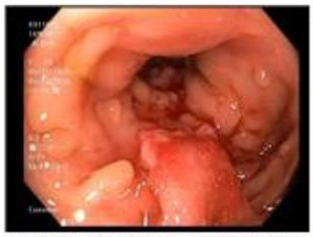
No obvious active mucosal inflammation



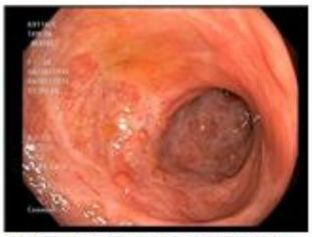
Polyp (8 mm to 10 mm) in the sigmoid colon



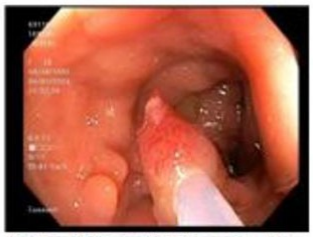
Polyp (12 mm to 14 mm) in the sigmoid colon



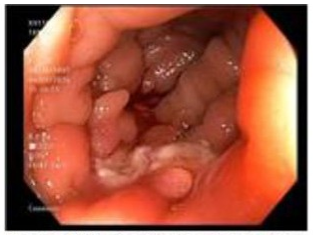
Polyp (12 mm to 14 mm) in the sigmoid colon



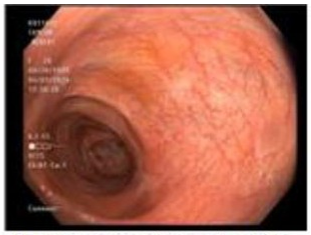
Mild scar tissue from previous inflammation in the rectum sigmoid and descending region



Polyp (12 mm to 14 mm) in the sigmoid colon



Polyp (12 mm to 14 mm) in the sigmoid colon



Normal-appearing rectum with representative biopsies

Upon followup colonoscopy above which was after the enzyme protocol, they noted no obvious mucosal inflammation, mild scar tissue from previous inflammation in the rectum sigmoid and descending region, internal hemorrhoids, a single sessile polyp of benign appearance ranging in size from 8 mm to 10 mm in the sigmoid colon at 30 cm from the anus which was oozing and had mild inflammation. The mucosa around it was normal and the polyp was removed using a hot snare. There was a single pedunculated polyp of benign appearance with stigmata of recent bleeding ranging in size from 12 mm to 14 mm noted in the sigmoid colon at 25 cm from the anus, and the area appeared to have either congestion mucosal or possible villous features and it too was removed. The patient's UC was deemed to be in endoscopic remission and the patient was recommended a followup colonoscopy a year later.

PROTOCOL

Based on Transformation's Thrive in 63 program, the enzyme protocol used in this case study is designed to gently introduce enzymes and probiotics with the DigestZyme, GastroZyme, PureZyme, and Plantadophilus formulations from Transformation's Genesis of Good Health® product line formulated with sensitive individuals in mind. Once the patient is ready to progress onto Transformation's Professional Protocol™ product line, the Digest, Gastro, Protease, and Probiotic formulations are recommended for their therapeutic value through the duration of the program. The benefits of enzyme therapy in the case of Ulcerative Colitis is multifold, and the types of dietary supplements used in this case study fall into four categories: digestive support with enzymes, mucosal lining support with enzymes and herbs, inflammatory and immune support with proteolytic enzymes and microbiome support with probiotics. Digestive enzymes with meals help ensure proper assimilation and bio-availability of all nutrients supporting cellular health and repair of the mucosal lining. Complete digestion also minimizes food intolerances and supports a healthy immune system.

- DigestZyme is a gentle yet comprehensive enzyme blend containing carbohydrases, protease, and lipase with the probiotics *L. acidophilus* and *B. longum*.

- Professional Protocol™ Digest is a comprehensive and therapeutic enzyme blend high in lipase, protease, and carbohydrases to ensure complete digestion of all foods.

An enzyme-delivered herbal and nutritional support formula after meals helps soothe GI discomfort and heal damaged mucosal lining of the GI tract, respiratory system, and urinary system.

- GastroZyme is an herbal formula with marshmallow root, papaya, prickly ash, and gotu kola plus enzymes, all to heal and repair the mucosal lining.

- Professional Protocol™ Gastro is a comprehensive and therapeutic herbal and enzyme formula designed to support digestion and reduce digestive discomfort.

A protease formula taken with meals assists with protein digestion and taken between meals helps promote optimal blood flow and efficient detoxification as well as helps manage inflammation, supporting the overall health of all systems of the body.

- PureZyme is a gentle protease formula with calcium that provides additional support for enhanced protein digestion when taken along with the digestive enzyme formula above. Taken at bedtime or away from meals, PureZyme supplies protease enzyme support to promote healthy circulation, immunity, inflammatory control, and detoxification.

- Professional Protocol™ Protease is a comprehensive and therapeutic blend of acid / alkaline / neutral proteases and peptidases that targets complete protein digestion when taken with meals. Taken at bedtime or away from meals, Protease supplies a comprehensive and therapeutic blend of proteolytic enzymes for systemic benefits.

A probiotic supplement further supports digestion and a strong immune system while maintaining a healthy gut environment.

- Plantadophilus is a single strain probiotic *L. plantarum* totaling 2 billion cfu per capsule to begin repopulating healthy gut flora.

- Professional Protocol™ Probiotic is a therapeutic formula with 6 strains of probiotics totaling over 5 billion cfu per capsule to support repopulation of a healthy microbiome.

DISCUSSION

Conventional treatment for UC is based on both the extent of the disease and its severity. Rectal application of medical therapy via suppositories or enemas is usually the first line of treatment. These can include anti-inflammatory medications, steroids, immune system suppression medications, and biological therapies. These medications generally work by blocking the inflammation in the body in various ways and putting the inflammation into "remission." Most drug development efforts currently focus on blocking the inflammatory cascade, which most likely is, at least in part, a secondary rather than a primary event. While these medications can provide symptom relief, they do not address root cause and can be accompanied with unwanted side effects. Proteolytic enzymes are safe alternatives to inflammation due to their adaptive ability to listen to the body to properly upregulate and downregulate the production of various inflammatory markers as needed. Proteolytic enzymes having anti-inflammatory properties along with other digestive enzymes and probiotics that ensure optimum digestion and absorption of nutrients as well as facilitating removal of waste may be a novel therapy for conditions such as UC. Transformation Enzyme Corporation's Thrive in 63 protocol contains enzyme and probiotic formulas to support healthy GI function to assure optimal protein digestion and proper blood flow necessary for effective nutrient delivery, a healthy immune response, and the body's natural detoxification processes. Our clinical observation shows Transformation's Professional Protocol™ Protease, a main constituent of the Thrive in 63 protocol, is a high value enzyme in the therapeutics field as it is an effective treatment for inflammation making it beneficial for someone with UC. As a natural and nontoxic compound, enzymes can be used as an alternative to multiple chemical ingredients and artificially manufactured medicines. These beneficial health properties of mucilaginous herbs, enzymes, and probiotics are what we consider to be the key in supporting conditions such as UC since it is a relapsing and remitting IBD characterized by mucosal inflammation. In this case study, the patient started the program with the Thrive in 63 protocol and transitioned from the Protease capsules to the Protease powder (5 grams three times daily) for the remaining of the study on the fifth month. The patient's symptoms waxed and waned throughout the protocol and finally stabilized resulting with complete remission of UC.

CONCLUSION

Here we have a 28-year-old female patient with severe UC which began in November 2020 and was confirmed via colonoscopy in October 2022. The patient complained of blood and mucus in the stool which occurred 15 or more times a day. She experienced frequency / urgency of bowel movements and diarrhea accompanied by sharp abdominal left lower pain daily. She also experienced hair loss, achy joints, anxiety, GERD, bloating, depression, anemia, eczema, chronic fatigue, shortness of breath, headaches, poor concentration, and brain fog. She had been taking Vyvanse® for 8 years for ADHD, Xyzal® for 8 years for allergies, Omeprazole for 2 years for GERD, and Ogestrel® for 2 years for irregular menses. Her ability to eat a variety of foods without experiencing acute symptoms was very limited, and despite this limitation she was unable to lose weight and

weighed 165 lbs. All end points were met as we observed through imaging studies healing of the ulceration and decreased GI inflammation as well as improvement of bowel movements from constant bloody diarrhea to normal fecal matter, decreased pain, and improved tolerance to a variety of foods without causing distress. The patient reported not having to take Omeprazole after not being able to live without it for 2 years, and she also discontinued the Ogestrel® for the irregular menstrual cycles she had experienced in the past. The patient was able to return to a daily exercise regimen at the gym, lost 23 lbs, and states she feels "great." This case study sheds light on enzyme and probiotic therapy having anti-inflammatory properties and ensuring optimum digestion and absorption of nutrients as well as facilitating removal of waste, which indicates it may be a novel therapy for IBD including UC.

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