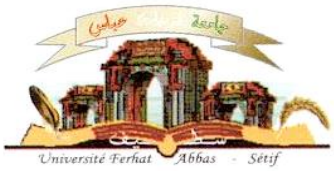
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Natural Remedies for Managing Crohn's Disease: *Curcuma Longa* and *Verbena Officinalis*

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JURY

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We embarked on the beginnings only by His guidance, and we reached the ends only by His grace, and we achieved the goals only by His favor. So, O ***Allah,*** *praise be to You until You are pleased, praise be to You when You are pleased, and praise be to You after You are pleased.*

I dedicate the fruit of my success to

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« It is a beautiful thing for a person to strive for success and achieve it, and even more beautiful to remember those who were the reason for it. »

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To the one who has been my support in good times and bad ones, to the one who worked hard and took care of my upbringing, to the one who showered me with her love, affection, and kindness, to the one whose virtues words cannot describe, to the one under her feet paradise lies, my beloved and precious mother ***Farida***

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To those who intended to break us, may ***ALLAH*** *make them a bridge for us to cross towards better things.*

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ملخص

مرض كرون هو حالة التهابية مزمنة تؤثر غالبًا على الجزء العلوي من الأمعاء الدقيقة والأمعاء الغليظة، وتتميز بفترات من التصاعد والتلاشي للأعراض، يعد الكركم مادة مهمة. يتم استخدام الكركم بشكل رئيسي لاستخراج الكركمين، وهو مركب طبيعي نشط يأتي من جذر الكركم. الكركمين معروف بفعاليته البارزة كمضاد للالتهابات ومضاد للأكسدة، وأظهرت الأبحاث أنه يمكن أن يكون له تأثيرات إيجابية على الصحة، مثل تقليل التورم، تخفيف الألم، ودعم الصحة العامة للجهاز المناعي والهضمي. بالإضافة إلى ذلك، اللويزة هي نبات عشبي يُستخدم في الطب العشبي لتهدئة الأعصاب، وتقليل القلق، وتحسين عملية الهضم، وتخفيف الاضطرابات المعوية البسيطة، كما أن لها خصائص مضادة للالتهاب. وفقا لدراسة إحصائية موجهة لمرضى كرون أظهرت أن اغلبية المرضى حوالي 52.4% يستعملون الكركم في تخفيف الالتهاب وحدة المرض، كما ان 59.1% يستعملون اللويزة في تخفيف الألم والمضاعفات المعوية وبالتالي في ولاية سطيف الكركم واللويزة تعتبر خيارات مفيدة ومحتملة كجزء من نهج شامل لإدارة وعلاج مرض كرون.

الكلمات المفتاحية: الجهاز الهضمي، الكركم،.اللويزة, مرض كرون

Abstract

Crohn's disease is a chronic inflammatory condition that often affects the upper part of the small intestine and the colon, characterized by periods of flare-ups and remission of symptoms. *Curcuma Longa* is considered a significant substance in this regard. It is primarily used to extract curcumin, a natural active compound derived from the turmeric root. Curcumin is well-known for its prominent anti-inflammatory and antioxidant properties, with research indicating potential positive effects on health such as reducing swelling, alleviating pain, and supporting overall immune and digestive health. Additionally, *Verbena Officinalis* is an herbal plant used in herbal medicine to calm nerves, reduce anxiety, improve digestion, and alleviate minor gastrointestinal disorders, also possessing anti-inflammatory properties. According to a statistical study focused on Crohn's disease patients, it was shown that the majority of patient about 52.4% use turmeric to alleviate inflammation and disease severity, as well as 59.1% use *Verbena* to alleviate pain and intestinal complications. Therefore, in Setif, *Curcuma Longa* and *Verbena Officinalis* are considered useful and potential options as part of a comprehensive approach to managing and treating Crohn's disease.

Keywords: Crohn's disease, *Curcuma Longa*, Digestive System, and *Verbena Officinalis.*

Résumé

La maladie de Crohn est une affection inflammatoire chronique qui affecte souvent la partie supérieure de l'intestin grêle et le côlon, caractérisée par des périodes de poussées et de rémission des symptômes. Le *curcuma Longa* est une substance importante dans ce contexte. Il est principalement utilisé pour extraire la curcumine, un composé actif naturel dérivé de la racine de curcuma. La curcumine est bien connue pour ses propriétés anti-inflammatoires et antioxydantes marquées, avec des recherches indiquant des effets positifs potentiels sur la santé tels que la réduction de l'enflure, le soulagement de la douleur et le soutien de la santé globale du système immunitaire et digestif. De plus, *Verbena Officinalis* est une plante herbacée utilisée en médecine traditionnelle pour apaiser les nerfs, réduire l'anxiété, améliorer la digestion et soulager les troubles gastro-intestinaux mineurs, tout en possédant également des propriétés anti-inflammatoires. Selon une étude statistique axée sur les patients atteints de la maladie de Crohn, il a été démontré que la majorité des patients 52.4% utilisent le curcuma pour soulager l'inflammation et la sévérité de la maladie, ainsi que 59.1% utilisent *Verbena Officinalis* pour soulager la douleur et les complications intestinales. Ainsi, à Sétif, le curcuma et *Verbena Officinalis* sont considérés comme des options utiles et potentielles dans le cadre d'une approche globale pour la gestion et le traitement de la maladie de Crohn.

Mots clé : Curcuma Longa, Maladie de Crohn, système digestif, et *Verbena Officinalis.*

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LIST OF ABBREVIATIONS

CD: Crohn's disease

CT: Computed tomography

DCs: Mucosal dendritic cells

IBD: Inflammatory bowel diseases

IDK : I don’t know

IL: Interleukine

INF: Interferon

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INTRODUCTION

Introduction

Crohn's disease is a chronic inflammatory condition that primarily affects the gastrointestinal tract. It is classified as an inflammatory bowel disease along with ulcerative colitis. Crohn's disease can affect any part of the digestive tract, from the mouth to the anus, but most commonly involves the small intestine and the beginning of the large intestine (colon). The exact cause of Crohn's disease is not fully understood, but it is believed to involve a combination of genetic predisposition, immune system dysfunction, and environmental factors. Symptoms of Crohn's disease can vary widely but often include abdominal pain, diarrhea (which may be bloody), fatigue, weight loss, and in severe cases, complications such as bowel obstruction, abscesses, or fistulas.

Management of Crohn's disease typically involves medications to suppress inflammation and modulate the immune response, dietary adjustments, and in some cases, surgery to remove damaged portions of the intestine. Crohn's disease is a lifelong condition with periods of remission and flare-ups, and treatment aims to alleviate symptoms, reduce inflammation, and improve quality of life for affected individuals.

Phytotherapy, using medicinal plants, offers a complementary approach to managing Crohn’s disease, a chronic inflammatory bowel disease. Plants such as turmeric, rich in curcumin, as well as verbena officinalis, are recognized for their anti-inflammatory properties. These plants help reduce inflammation and symptoms associated with Crohn’s disease. However, it is essential to consult a healthcare professional before integrating phytotherapy into treatment to avoid drug interactions and side effects.

This work aims to present the current knowledge from the scientific literature on the use of turmeric and Verbena officinalis in treating IBD. We will begin by outlining the digestive system and inflammatory bowel diseases, focusing on Crohn's disease. Next, we will introduce *Curcuma longa* and *Verbena officinalis*, discussing their physiology, phytochemistry, pharmacological significance, and active molecules. Finally, we will delve into and analyze the survey results.

DIGESTIVE SYSTEM

I.Generalities

Delving into the wonders of the human body, one can't help but marvel at the intricacies of the digestive system, a finely tuned network of organs devoted to processing the food we consume. Its anatomy encompasses a fascinating array of structures, from the intricate folds of the small intestine to the muscular contractions of the esophagus (Law *et al*., 2002). But it's not just about form; the physiology of the digestive system involves a symphony of chemical reactions, enzymes, and hormones orchestrating the breakdown of food into nutrients our bodies can use. From the moment food enters the mouth to its journey through the stomach, small intestine, and beyond, each step is finely tuned to extract essential nutrients and energy while discarding waste. Understanding the anatomy and physiology of the digestive system offers profound insights into the intricate workings of our bodies and the remarkable processes that sustain life (Fieker *et al*., 2011).

II. The Digestive Tract

The digestive system is a collection of organs and glands within the human body that work together to process food, extract nutrients, and eliminate waste. It begins with the ingestion of food and ends with the expulsion of indigestible material as feces. Key components of the digestive system include the mouth, esophagus, stomach, small intestine, large intestine, liver, gallbladder, and pancreas (Fig1). Through mechanical and chemical processes, the digestive system breaks down food into molecules small enough to be absorbed by the body, providing essential nutrients and energy for cellular function and growth (Jonathan, 2014).

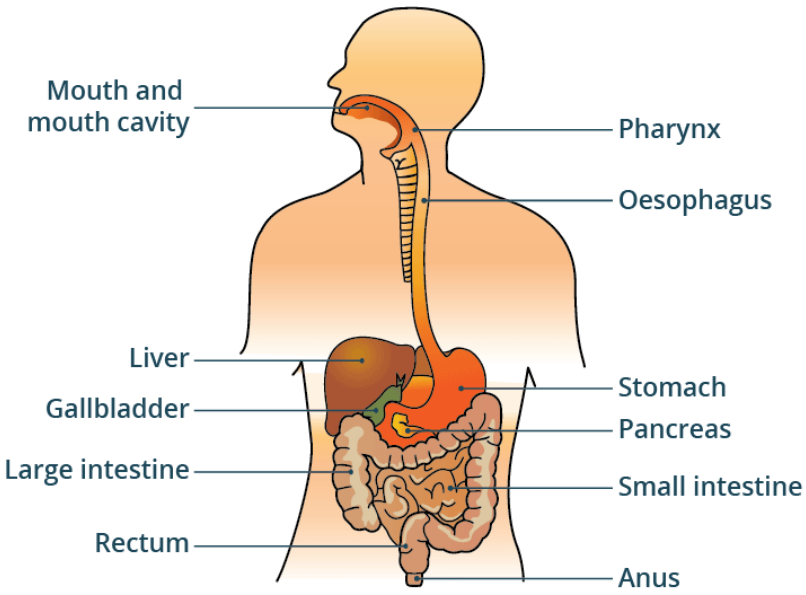


Fig. 1: Anatomy of the human digestive system(https://www.istockphoto.com)

III. Anatomy of the Digestive Tract

III.1. Layers and Structure

The digestive tract is a hollow tube that extends from the mouth cavity to the anus. Starting from the esophagus, the digestive wall consists of four concentric layers (Fig. 2), which are, from the inside out, the mucosa, the submucosa, the muscularis, and the adventitia (Garrett, 2018).

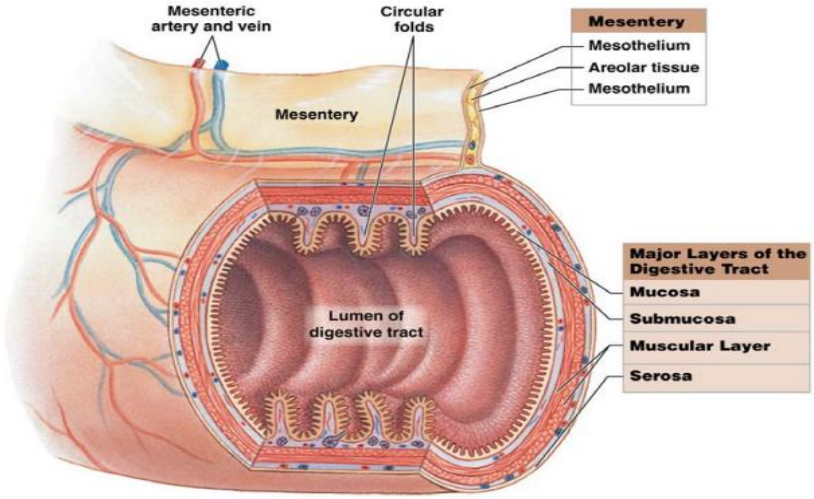


Fig. 2: Anatomy of the Digestive Tract: Four Layers of Structure (Garrett, 2018).

III.1.1. Mucosa

Mucosais delimited by an epithelium whose type corresponds to the function of the segment, located above a chorion composed of loose connective tissue, highly vascularized, rich in immune cells organized into lymphoid formations whose importance and arrangement are variable, and provided with exocrine glands whose structure varies depending on the segments considered (Fig. 3). The mucosa terminates in the muscularis mucosae, formed of smooth muscle cells (Garrett, 2018).

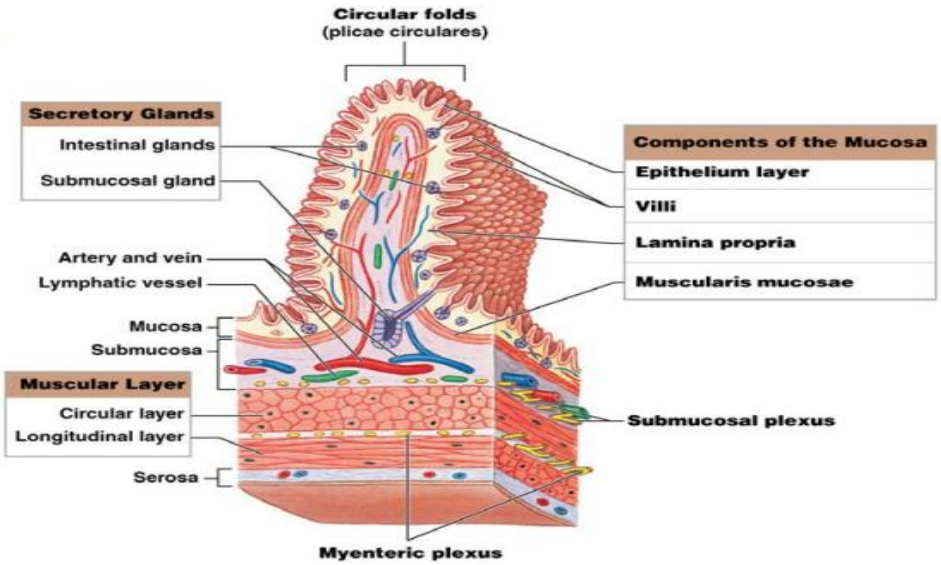


Fig. 3: Components of the mucosa (Garrett, 2018).

III.1.2. Submucosa

Submucosais composed of a denser connective tissue containing blood vessels and a network of sympathetic nerves, the Meissner's plexus, which controls the motility of the digestive tract (Fig.4). It is in this layer that we find the lymphoid follicles of the lymphoid organs associated with the digestive tract (Peyer's patches of the ileum and appendix) and the glands of the duodenum(Garrett, 2018).

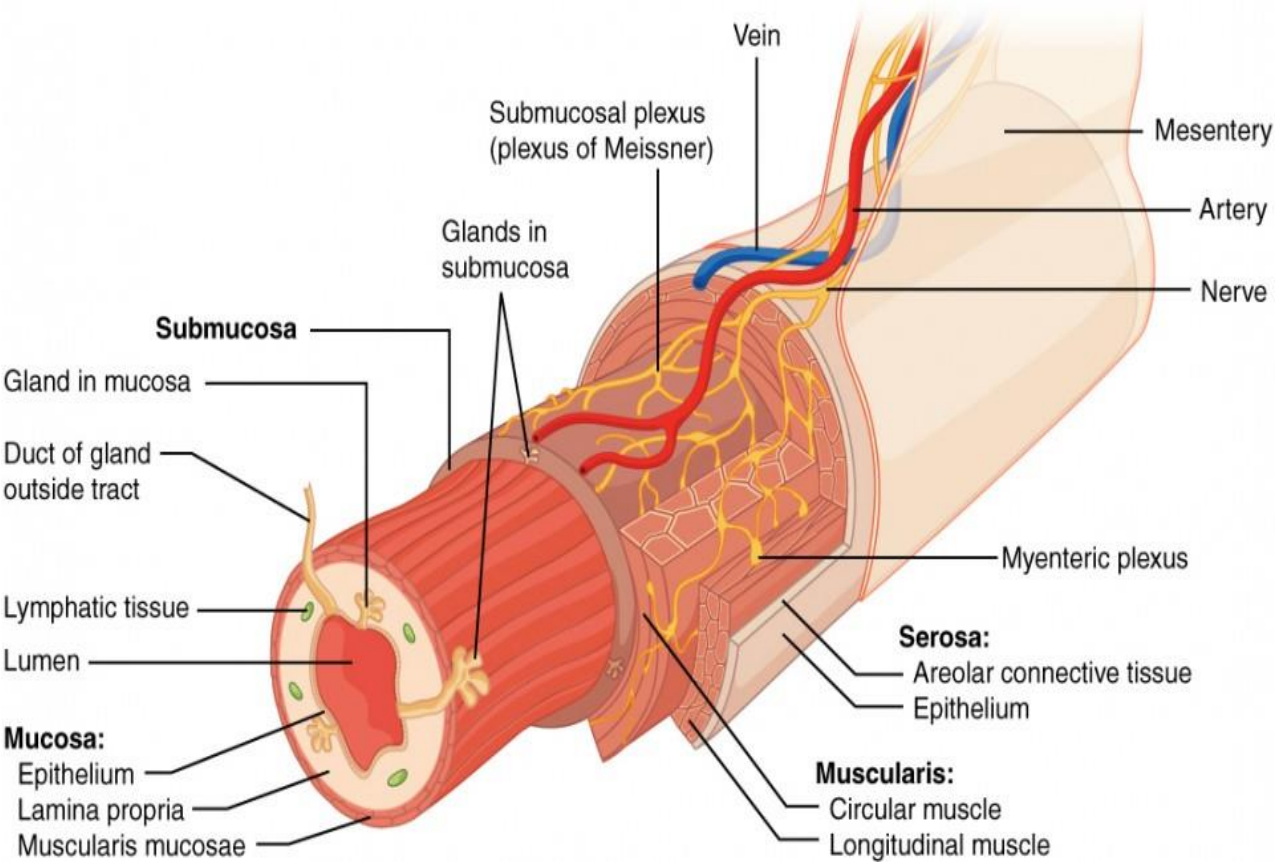


Fig. 4: General structure of the digestive tract (https://fr.m.wikipedia.org).

III.1.3. Muscularis

Muscularis is composed of smooth muscle cells arranged in two axes, forming an inner circular layer and an outer longitudinal layer (Fig.4). Between them, nerve plexuses, the Auerbach's plexus, ensure the vegetative innervation of the digestive tract (Garrett, 2018).

III.1.4. Adventitia or serosa

Serosa is a layer of vascularized dense connective tissue containing numerous adipocytes. This layer ends with a mesothelium, which is the visceral layer of the peritoneum (Garrett, 2018).

III.2. Elements of the digestive tract

The digestive system is a marvel of biological engineering, comprising several essential structures that work together seamlessly to process food and extract nutrients. Here are some key components of this intricate system (Ferguson, 1990; Atenodoro and Ruiz,2019):

- **The Oral Cavity**: Serving as the initial entry point of the digestive tract, the mouth plays a pivotal role in both mechanical and chemical digestion. It encompasses various structures such as the teeth, lips, tongue, palate, uvula, and cheeks (Ferguson, 1990).
- **The Stomach**: Positioned beneath the left side of the diaphragm in the abdominal cavity, the stomach is a sizable, muscular organ resembling a bean. Its primary function revolves around the storage of food (Atenodoro and Ruiz,2019).
- **The Small Intestine**: Often hailed as the most critical segment of the digestive tract, the small intestine serves as the epicenter for digestion and absorption. It is here that the majority of nutrient breakdown and absorption occur, making it a vital site for nourishing the body (Atenodoro and Ruiz,2019).
- **The Large Intestine**: Comprising the cecum, colon, appendix, rectum, and anus, the large intestine follows the small intestine in the digestive journey. Though primarily associated with water absorption and waste elimination, it plays a crucial role in maintaining overall digestive health (Atenodoro and Ruiz,2019).

These components, each with its unique functions, collectively contribute to the intricate process of digestion, ensuring the body receives the essential nutrients required for optimal functioning (Ferguson, 1990; Koepsell, 2020).

III.3. Accessory glands of the digestive system

The digestive system also includes organs located outside of the digestive tract (Atenodoro and Ruiz, 2019):

- **Liver**: It is the largest organ in the human body (a large, amphicrine, homotypic gland), and in a certain sense, the most complex. It is positioned in a diversion on the venous circulation and acts as a filter. It serves as the body's chemical factory and has numerous vital functions: it regulates the levels of chemicals in the body, synthesizes blood clotting factors in case of bleeding. In terms of digestion, its role is primarily the secretion of bile.

This bile is thus stored in the gallbladder, which is attached to the liver and connected to the digestive tract (Atenodoro and Ruiz, 2019).

- **Pancreas:** It's a heterotypic amphicrine gland (both endocrine and exocrine) composed of distinct elements. The exocrine pancreas elaborates enzymes, zymogens, and the endocrine pancreas secretes hormones that regulate carbohydrate metabolism (Bragado *et al*., 2000). It contains two types of glandular tissue: pancreatic acini that produce digestive enzymes like amylase, lipase, and trypsin, and the Islets of Langerhans that produce two antagonistic hormones, insulin and glucagon (Ferguson, 1990).

IV. Function

The function of the digestive system is to digest and absorb food and then excrete the waste products with the help of the liver, gallbladder, pancreas, small intestine, large intestine, and rectum. Each of these organs plays a specific role in the digestive system (Nikaki and Gupte, 2016).

IV. 1. Oral cavity

The oral cavity has four main functions. First, it provides sensory analysis of food material before swallowing and mechanical processing via the action of the teeth, tongue, and palatal surfaces. The oral cavity also provides lubrication by mixing food material with mucus and salivary gland secretions and limited digestion of carbohydrates and lipids (Visentin *et al*., 2014).

Functions of the tongue include mechanical processing of food material by compression, abrasion, and distortion; manipulation to assist in chewing and preparing material for swallowing; sensory analysis by touch, temperature, and taste receptors; and secretion of mucins and lingual lipase. The lingual lipase has a broad pH and breaks down lipids (mainly triglycerides). A pH of 3.5 to 6 allows lingual lipase to work even in the stomach's acidic environment (Bragado *et al*., 2000; Nikaki and Gupte, 2016).

Within the oral cavity, there are three pairs of salivary glands. The first pair is the parotid salivary glands located inferior to the zygomatic arch and posterolateral to the mandible. The parotid glands produce serous secretions containing a large amount of salivary amylase, which breaks down carbohydrate complexes. Next are the sublingual salivary glands located on the floor of the mouth (Fish *et al*., 2022). The sublingual glands produce a mucous secretion that serves as both a buffer and lubricant. The third is the submandibular salivary glands, located on the floor of the mouth within the mandibular groove. They function by secreting a mixture of buffers, glycoproteins called mucins, and salivary amylase (Visentin *et al*., 2014).

Altogether, these glands produce 1.0 to 1.5 liters of saliva each day. Close to 99.4% of the saliva produced is water, and the remaining 0.6% consists of electrolytes, buffers, glycoproteins (mucins), antibodies, enzymes, and waste products. These function to lubricate the mouth to prevent friction between the mucosa of the oral cavity and the food material, moisten the food material for easy swallowing, and initiate lipid and carbohydrate complex digestion (Volk and Lacy, 2017).

The teeth provide a mechanical breakdown of food materials; for instance, the connective tissue of meat and plant fibers in vegetables. This process also saturates the salivary secretions and enzymes within the food material for better digestion (Nikaki and Gupte, 2016).

IV.2. Pharynx

The pharynx serves as a passageway of food material to the esophagus. During swallowing, closure of the nasopharynx and larynx occurs to maintain the proper direction of food; a process achieved by cranial nerves IX and X. From the pharynx, food material goes to the esophagus (Fish *et al*., 2022).

IV.3. Esophagus

The primary function of the esophagus is to transport food materials into the stomach via waves of contraction of its longitudinal and circular muscle, known as peristalsis. The upper one-third of the esophagus is predominantly skeletal muscle, the middle one-third is a mixture of skeletal and smooth muscle, and the lower one-third is primarily smooth muscle. However, during deglutition, the buccal phase is the only voluntary phase where one can still control the swallowing process (Volk and Lacy, 2017). The skeletal muscles in the pharynx and upper esophagus are controlled by the swallow reflex; hence the pharyngeal and esophageal phases of swallowing are under involuntary control via afferent and efferent fibers of glossopharyngeal and vagus nerves. The smooth muscles of the esophagus are arranged circularly and longitudinally and aid in peristaltic movement during swallowing (Kong *et al*., 2018).

IV.4. Stomach

Once the food material arrives in the stomach, it can be temporarily stored and mechanically and chemically broken down by the actions of stomach acids and enzymes. The secretion of intrinsic factor produced by the stomach helps appropriately absorb vitamin B12(Nikaki and Gupte, 2016). The ability of the stomach to store food stems from its compliance and ability to change size. On average, the lesser curvature of the stomach has a length of approximately 10 cm, and the

larger curvature has a length of roughly 40 cm. The stomach typically spans from vertebrae T7 to L3, giving it the ultimate ability to hold on to a large amount of food (Volk and Lacy, 2017).

The ability of the stomach to mechanically break down food materials is due to its sophisticated muscular dimensions. The stomach has three muscular layers: an inner oblique layer, a middle circular layer, and an external longitudinal layer. The contraction and relaxation of these three muscular layers of the stomach assist in the mixing and churning activities essential in the formation of chyme. Then the chemical breakdown of food material in the stomach is propagated by the gastric glands, produced majorly by the parietal cells, chief cells, G-cells, foveolar cells, and mucous neck cells (Fish *et al*., 2022).

The parietal cells secrete intrinsic factors and hydrochloric acid. The intrinsic factor produced is essential in the absorption of vitamin B12. It binds to B12, allowing for proper absorption at the ileum of the small intestine (Koepsell, 2020). The hydrochloric acid produced by the parietal cell keeps the stomach pH between 1.5 to 2.0. The stomach acidity brought on by hydrochloric acid destroys most of the microorganisms ingested with food, denatures protein, breaks down plant cell walls, and is essential for the activation and function of pepsin, a protein-digesting enzyme secreted by chief cells (Drucker *et al*., 2011). The chief cells produce a zymogen called pepsinogen, which gets activated at a pH between 1.5 to 2 to become pepsin. Pepsin is a protein-digesting enzyme. The foveolar and mucous neck cells produce mucous, protecting the gastric epithelium from acidic corrosion (Kong *et al*., 2018). The G cells are abundant within the pyloric section of the stomach. They produce gastrin which stimulates secretions from the parietal and chief cells. Within the pyloric glands of the stomach, D cells produce somatostatin, which inhibits gastrin release (Qin and Pei, 2018).

IV.5. Small intestine

Chyme is directed to the small intestine, where digestion continues. Unlike the stomach, which has minor absorptive properties, 90% of food absorption occurs in the small intestine. The small intestine has three segments: the duodenum, the jejunum, and the ileum. The duodenum receives chyme from the stomach and digestive material from the pancreas and the liver (Koepsell, 2020). The jejunum is where the bulk of chemical digestion and absorption occur. The ileum also has digestion and absorption functions. The ileum is the last segment of the small intestine and contains the ileocecal valve, a sphincter that controls the flow of material from the ileum to the cecum of the large intestine (Fish *et al*., 2022).

The small intestine mucosa has villi, and each villus has multiple microvilli, which increase the surface area for optimal absorption (Law *et al*.,2002). There are extensive networks of capillaries

within the villi that carry absorbed nutrients to the hepatic portal circulation. Also, many lymphatic capillaries called lacteals aid in chylomicron transportation to the venous circulation (Kong *et al*., 2018).

The intestine has both endocrine and exocrine glands that produce hormones, enzymes, and alkaline mucinous material. Some hormones released by the small intestine are listed below (Drucker *et al*., 2011; Koepsell, 2020).

- Gastrin produced by G-cells in the upper small intestine (but primarily found in the stomach)
- Cholecystokinin produced by I-cells in the upper small intestine
- Secretin produced by S-cells in the upper small intestine in response to decreased upper intestine pH
- Gastric inhibitory peptide produced by K-cells in the upper small intestine in response to fat, amino acids, and glucose
- Pro-glucagon produced by L-cells in the distal ileum and colon in response to glucose and fat
- Somatostatin produced by D-cells in the small intestine, including the stomach and pancreas
- Vasoactive intestinal polypeptide produced by parasympathetic ganglia in the small intestine in response to distension
- Motilin produced by M-cells in the upper small intestine

The enzymes produced by the small intestine include lipase for fats digestion, peptidase for peptide breakdown, and sucrase, maltase, and lactase for sucrose, maltose, and lactose breakdown, respectively. Brunner glands, primarily found in the duodenum, produce bicarbonate for acid neutralization (Drucker *et al*., 2011).

IV.6. Accessory glands of the digestive system

Within the duodenum, accessory digestive organs such as the liver and the pancreas release digestive secretions. The liver is the largest internal organ and gland in the human body. It has numerous functions, but as an accessory organ of the digestive system, it produces bile which emulsifies fats and various lipids for optimal digestion. Bile produced in the liver is stored in the gallbladder. The gallbladder contracts to release bile into the duodenum when fat-containing food is present (Vegesna *et al*., 2012).

The pancreas also has exocrine glands that are essential for the food digestion process. The exocrine glands of the pancreas produce multiple enzyme precursors and enzymes, which include trypsinogen, chymotrypsinogen, and procarboxypeptidase, which are activated by enteropeptidase in the small intestine; active alpha-amylase; lipases and colipase, which act on triglycerides and phospholipids; and several other enzymes like ribonuclease, elastase, and collagenase (Fieker *et al*., 2011).

IV.7. Large intestine

The unabsorbed and undigested food material progresses to the large intestine. At this point, it is called feces. The large intestine is about six feet long and comprises the cecum, ascending colon, transverse colon, descending colon, and sigmoid colon. The large intestine absorbs water and electrolytes (Flemströmand Isenberg, 2021). Also, due to the trillions of microbes that live in the large intestine, these organisms can break down undigested food material. In addition, nutrients such as vitamin K are produced and absorbed in the large intestine. The peristaltic movement of the large intestine moves the feces into the rectum. In the rectum, stretch receptors signal for the defecation process to start, which includes a reflexive relaxation of the internal anal sphincter smooth muscle and conscious relaxation of the external anal sphincter skeletal muscle (Law *et al*., 2002; Liao *et al*., 2014).

V. Gastrointestinal System Disorders

Gastrointestinal system diseases can affect anywhere from the mouth to the anal canal and can be caused by any number of things. For example, abnormalities of the oral cavity include salivary gland tumors such as pleomorphic adenoma, mucoepidermoid carcinoma, and Warthin tumor, all of which affect proper salivary content and production (Dibong *et al*., 2020).

Further along the gastrointestinal tract, gastritis involves inflammation of the stomach. This condition can vary, depending on the duration of symptoms. Gastritis may have an acute onset caused by NSAIDs or mucosal ischemia. Chronic causes of gastritis are typically due to *Helicobacter pylori* or autoimmune disease (Krause, 2009). One such cause of autoimmune disease is pernicious anemia, a condition preventing either the proper formation of intrinsic factor or its binding to vitamin B12, a nutrient vital in physiologic processes such as DNA and RNA synthesis, hematopoiesis, and neurologic function. Vitamin B12 deficiency can also be attributed to a lack of dietary intake, as the nutrient must be acquired through animal products or supplemented food sources (Nicosia *et al*., 2021).

Diseases of the small and large bowel include celiac disease, tropical sprue, Whipple disease, Crohn disease, and ulcerative colitis, which impact digestion and absorption of food material. In addition to pathologic conditions, congenital disorders such as Hirschprung disease, biliary atresia, intestinal atresia, intestinal malrotation, and pyloric stenosis occur during infancy. They may be life-threatening as adequate nutrients cannot be absorbed (Volk and Lacy, 2017).

These diseases warrant proper workup starting with a thorough history and physical examination. Obtaining a history of present illness is essential to the diagnosis of gastrointestinal system disease and clarification of questions regarding the location and duration of the pain, radiation or changes in intensity, precipitating factors, associated symptoms such as fever, chills, nausea, vomiting, changes in bowel habitus, and stool color. Inquiries on any previous episodes of illness or related illnesses and prior surgeries, medication lists, and allergies are crucial (Nikaki and Gupte,2016; Kong *et al*., 2018).


Crohn's Disease

I. History of Crohn's disease

The disease known as Crohn's disease owes its name to the famous gastroenterologist, Dr. Burrill Crohn. It was first recognized as a medical condition when Crohn and his colleagues described it in 1932. However, the first explanation of Crohn's disease was provided by Giovanni Battista Morgagni (1682-1771). This Italian physician, considered the father of anatomopathology, indeed described the anatomoclinical history of a 20-year-old man suffering from chronic, sometimes bloody diarrhea and abdominal pain, who died from a perforation of the terminal ileum (Robertson, 2019).

In 1904, a Polish physician, Lesmowski, wrote a case report for a local medical journal, describing a patient with symptoms similar to those of CD. In 1913, an English author Combe, and a Scottish colleague, Daziel, reported several cases of "chronic interstitial enteritis" exhibiting characteristics of CD. However, these descriptions were completely ignored by the academic world (Tersigni and Prantera, 2010). It was believed that Crohn's disease exclusively affected the small intestine until 1960, when Lockhart-Mummery and Basil Morson (a pathologist at Mark's Hospital, London) described involvement of the large intestine by Crohn's disease (Day *et al*., 2003). It was also in the 1950s that the anal and ano-rectal manifestation was fully described (Morson and Lockhart-Mummery, 1959). Subsequently, it became clear that Crohn's disease could affect any part of the intestine, from the mouth to the anus, and that there could also be extraintestinal manifestations (Basu *et al*., 1974; Huchzermeyer *et al*., 1977).

II. Crohn's disease

Crohn's disease (CD) is an inflammatory condition of unknown etiology, clinically manifesting acutely, subacutely, or chronically, potentially affecting the entire digestive tract from the mouth to the anus but predominantly involving the intestines (Fig.5). It can occur at any age but typically begins in young adults, between 20 and 30 years old. Alongside Ulcerative Colitis and Indeterminate Colitis, it constitutes the Inflammatory Bowel Diseases (IBD). This condition is characterized by its occurrence in young adults, clinically by digestive symptoms, associated or not with systemic manifestations, and anatomically by lesions that can affect the entire digestive wall, resulting in transmural inflammation (Manouni, 2019).

While Crohn’s can affect any part of the digestive tract, it typically affects the small intestine and parts of the large intestine (colon). It can attack some parts of the digestive tract while skipping

over other parts. Ulcerative colitis only causes inflammation in the large intestineand does not skip sections of the tract (Sophia, 2023).

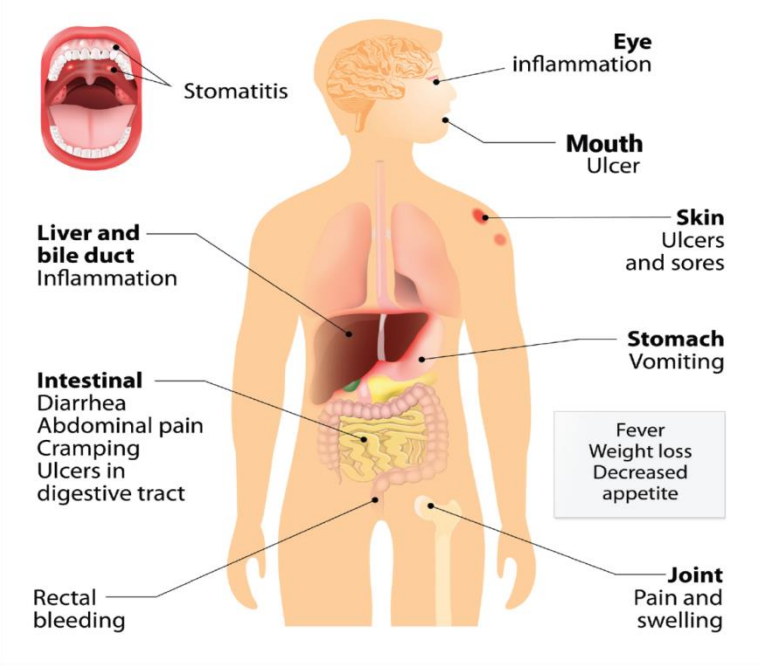


Fig.5: Signs and symptoms for crohn's disease (https://www.icare4u.health/crohns-disease).

Crohn's disease results from the occurrence, in the digestive mucosa, of an ab-normal inflammatory response elicited by an ostensibly normal luminal flora (Fig.6). Thus, the lesions appear to result from a breakdown in tolerance to the digestive flora, influenced by genetic and en-vironmental factors. There is no single model explaining entirely the process lead-ing to inflammation in Crohn's disease. The presumed links in this sequence consist of abnormalities in the barrier function of the digestive mucosa and the mucosal immune system (Bahadj *et al.*, 2019).

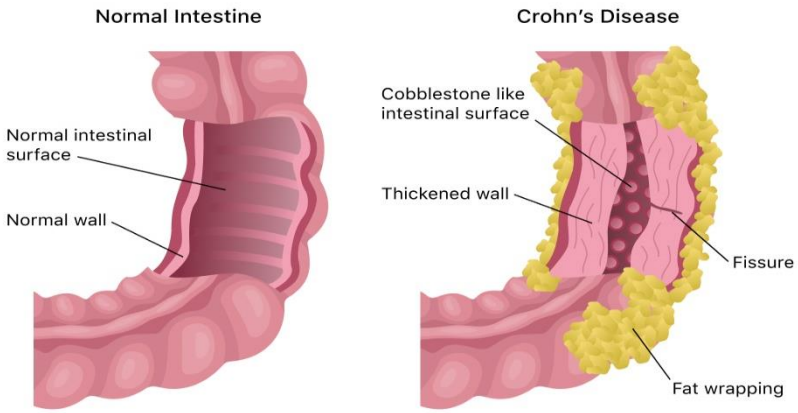


Fig. 6: Normal intestine and the intestine affected by Crohn's disease (https://www.health.harvard.edu).

III. Types of Disease

There are five types of Crohn's disease according to the Crohn's & Colitis Foundation. These are ileocolitis, ileitis, gastroduodenal Crohn's disease, jejunoileitis and Crohn's colitis (Fig.7.). Some medical centers recognize a sixth type called perianal disease. Each type affects a different part of the digestive tract and causes different symptoms and complications (Sophia ,2023).

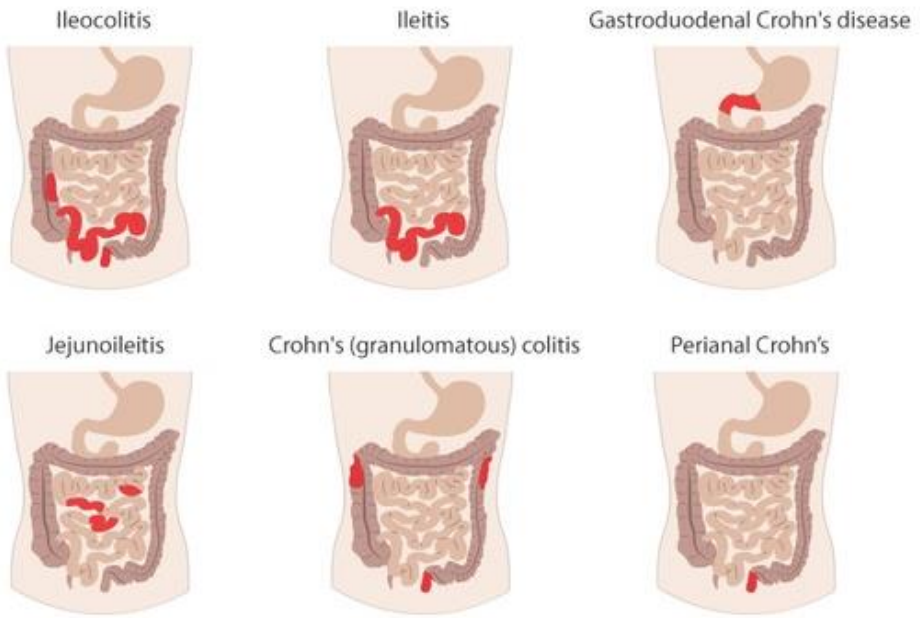


Fig. 7: Types of crohn's disease (https://www.ibdrelief.com/learn/what-is-ibd/what-is-crohns-disease).

III.1. Ileocolitis

Ileocolitis is the most common type of Crohn's disease, and it affects about 50 percent of patients. The end of the small intestine and the large intestine are affected (Fig.6). It causes pain in the lower and middle abdomen. Other symptoms include cramping, diarrhea and significant weight loss (Bayless *et al*., 1996).

III.2. Ileitis

Ileitis only affects the ileum, the last part of the intestine (Fig.6). About 30 percent of Crohn's patients experience this type. It has the same symptoms as ileocolitis, but severe cases may cause abscesses in the lower part of the abdomen and fistulas abnormal connections between two body parts, such as organs or blood vessels (Polito *et al*., 1996).

III.3. Gastroduodenal Crohn's Disease

Gastroduodenal Crohn's Disease is also called upper Crohn's disease, and it affects the stomach and the first part of the small intestine called the duodenum (Fig.6). This type is uncommon and affects about five percent of patients. Symptoms include vomiting, nausea, weight loss, loss of appetite and pain in the upper abdomen (Vineet *et al*., 2016).

III.4. Jejunoileitis

Jejunoileitis affects the upper half of the small intestine, called the jejunum (Fig.6). It causes patchy areas of inflammation and is uncommon. Symptoms include abdominal pain after eating that may be mild to intense, weight loss, diarrhea and malnutrition. In severe cases, fistulas may form (Jimmy *et al*., 2014).

III.5. Crohn's (Granulomatous) Colitis

Crohn's colitis only affects the large intestine (Fig.6), or colon, and affects about 20 percent of patients. Symptoms include rectal bleeding, abdominal pain, diarrhea and anal disorders such as abscesses and ulcers. People who have this type may also develop joint pains and skin lesions (Bengtson *et al*., 2009).

III.6. Perianal Disease

Perianal disease affects the anus-up (Fig.6) to one-third of Crohn's patients have this type of disease. Symptoms include fistulas, sores or ulcerations, abscesses and skin tags outside the anus (Vineet *et al*., 2016).

IV. Factors influencing the appearance of Crohn's Disease

The prevalence of CD has an incidence of 3 to 20 cases per 100,000 Crohn disease is more common in the industrialized world, particularly in North America and Western Europe, though the incidence is rising in Asia and South America.7,8 There may be a slightly higher predominance of CD in women and it is more common in individuals of Ashkenazi Jewish origin than in non-Jews. The exact pathogenesis of CD is unknown, although there are anumber of genetic and environmental factors that have been shown to increase the risk of the disease and lead to the aberrant gut immune response characteristic of the disease (Josepf *et al*.,2017).

IV.1. Tabacco

The most important environmental factor in CD, both in terms of prevalence and severity, is smoking. It increases the risk of developing CD (50 to 60% of patients are smokers at the time of diagnosis) and is crucial for the localization of lesions, with a higher prevalence for ileal involvement and lower prevalence for colonic involvement compared to non-smokers (Cortot *et al*., 2009). Furthermore, tobacco exacerbates CD. It increases the frequency of flare-ups and the need for corticosteroids and immunosuppressants. It is associated with more frequent intestinal complications and leads to significantly higher rates of clinical and surgical relapses (Nos *et al*., 2011).

The consumption of tobacco leads to an increase in the blood carbon monoxide levels and mucosal production of free radicals. Due to its pro-coagulant action, carbon monoxide promotes the formation of micro-thromboses in the intestinal wall, resulting in local ischemia and therefore exacerbation of lesions. Free radicals play a significant role in maintaining mucosal inflammatory reactions (Jimmy *et al*., 2014). Their action is normally modulated by the presence of antioxidants such as vitamin C, β-carotene, and α-tocopherol, which are deficient in smokers. Smoking cessation, therefore, has an undeniable beneficial effect on inflammatory bowel disease and this is evident from the first year. It is believed to have a comparable effect to an immunosuppressive treatment in terms of the risk of relapse (Jantchou *et al*., 2006; Nos *et al*., 2011).

IV.2. Presentation of the microbiotic world

There are approximately 100 trillion bacteria contained within the intestinal flora. Its composition varies according to the segment in which it is located. Indeed, in the stomach, its presence is very low due to the acidic pH of the stomach. Then, as it reaches the small intestine, the oxygen content decreases and the pH increases to about 6 (Jimmy *et al*., 2014). As a consequence, there is an increase in the number and profile of bacteria, which are aerobic-anaerobic with an increase in the number of anaerobes. In this zone, we find approximately 10^4 to 10^7 colony-forming units (CFU) per gram. In the colon, the levels increase to around 10^{11} CFU/g. This is the part of the digestive tract richest in anaerobic bacteria. The main reasons for this are primarily the slowing of transit and the very low redox potential. This abundance of microbial flora leads to significant production of metabolites, justifying its significant influence on carbohydrate, lipid, gas, and protein metabolism (Vineet *et al*., 2016; Nader, 2019).

Many studies have highlighted the presence of dysbiosis in CD. "Dysbiosis" refers to an imbalance between "protective" bacteria and "harmful" bacteria and is a current research avenue for understanding the pathophysiology of inflammatory bowel diseases. Meta-genomic analyses have revealed a disruption in the balance between deficient "protective" bacteria (such as Bifidobacteria, Lactobacilli, Faecalibacteriumprausnitzii) and increased "harmful" bacteria (including Bacteroides, adherent-invasive Escherichia coli, Enterobacter) in patients with CD (Driouich *et al*., 2017).

IV.3. Genetics factors

The existence of a genetic component in the pathogenesis of CD has been demonstrated in various ways. Firstly, several epidemiological studies have shown that the risk of developing CD is increased between 15 and 42 times for an individual with a first-degree relative (parent, sibling, child) affected by CD (Lanteri, 2019). As a result, scientists have sought genetic alterations in this disease. They discovered a mutation in the NOD2 gene (or CARD15), which shed new light on its pathophysiology. In healthy individuals, macrophages are the primary site of NOD2 gene expression. This gene codes for a protein belonging to a large family of cellular receptors. NOD2 enables the recognition of viral or bacterial elements by macrophages (Hugo *et al*., 2015).

The NOD2 protein binds with high affinity to bacterial peptidoglycans. Following this binding, the NOD2 protein undergoes dimerization and participates in an activation cascade, leading to the production of pro-inflammatory factors such as TNF-α. TNF-α is a pro-inflammatory cytokine that plays a key role in CD.TNF-α perpetuates a vicious cycle by continually activating the production and expression of other TNF-α molecules. Therefore, in patients with CD, TNF-α is detected in large quantities in intestinal lesions and in stool samples. The NOD2 variants associated with CD result in a loss of NOD2 function and thus a modification of macrophage response to bacteria (Kinani,2014). The NOD2 gene is also expressed in the epithelial cells of the intestinal mucosa, in the Paneth cells of colonic crypts, as well as in dendritic cells. The mutation of NOD2 is the most significant risk factor for Crohn's disease: one-third of patients carry this mutation. Mutations in the NOD2 gene are found in the heterozygous state in 30 to 40% of cases (15% in the general population) and in 15% of cases in the homozygous state (Chojnowska *et al*., 2018).

IV.4. Immunological factors

There is a pathophysiological model suggesting that Crohn's disease results from an inappropriate mucosal immune response against the disrupted intestinal flora of a genetically predisposed individual, in the presence of certain environmental factors. Thus, we observe a disruption of intestinal homeostasis (Atamnia and Meramria, 2019). Bacteria, or rather certain bacterial components, can induce an inflammatory response in two ways:

- Enter the mucosa and directly interact with the immune cells of the submucosa, such as dendritic cells or lymphocytes: this constitutes the adaptive immune response (Benrezkallah *et al*., 2017).
- In inflammatory bowel diseases (IBD), abnormalities in the innate immune response disrupt the recognition of antigens and their presentation to effector cells. Thus, the intestinal barrier becomes more sensitive to infections, and the activation of the mucosal immune system is dysregulated.

In Crohn's disease, Th1 lymphocytes are responsible for the secretion of interferon (IFN) and IL-12, initiating the inflammatory cascade with the production of TNF-α, IL-1β, and IL-6. From these foundations emerged the idea of therapeutic use of anti-TNF antibodies. Furthermore, recent research has uncovered a new population of T cells called Th17 cells, which may contribute to the predominance of effector populations over regulatory populations in IBD. These Th17 lymphocytes (CD_4+ CD_{25}^-) produce the pro-inflammatory cytokine IL-17, particularly in response to the presence of extracellular bacteria. The differentiation of the Th17 population from naïve T cells is induced by the co-expression of IL-23 and TGF-β, whose role in determining the balance between Treg (anti-inflammatory) and Th17 (pro-inflammatory) lymphocytes is crucial. The involvement of the IL-23R receptor gene in IBD has led to suspicion of this effector subpopulation, which exhibits strong inflammatory activity, allowing for the activation and local accumulation of neutrophils at the site of tissue inflammation and inducing the production of antimicrobial peptides such as human beta defensing (HBD) (Marion *et al*., 2019).

Directly stimulate the surface epithelium, notably through receptors related to pattern recognition receptors (PRRs): this constitutes the innate immune response (Benrezkallah *et al*., 2017). The weakening of the initial defenses of the intestinal mucosa contributes to the permeabilization of the intestinal epithelium, resulting in increased contact between commensal flora bacteria and the mucosal immune system. In CD, these interactions are facilitated by macrophages, whose secretion process of inflammatory cytokines may be defective. Excessive such interactions would lead to a loss of tolerance to commensal flora, activating the sentinel cells of the innate immunity:

mucosal dendritic cells (DCs), which are at the interface between intestinal epithelial cells and T lymphocytes.

In inflammatory bowel diseases, abnormal activation of DCs is observed at inflammatory sites, and the lack of Treg lymphocytes contributes to the development of an immune response against commensal bacteria that are normally tolerated. This loss of tolerance perpetuates inflammation. This abnormal activation of DCs is the main consequence of abnormalities in the functioning of Toll-like receptors (TLRs) and NOD receptors, which detect bacterial components (Marion *et al*., 2019).

However, another common immune anomaly in IBD has been recently identified. This involves the abnormal and increased expression of integrins by the intestinal vascular endothelium, allowing for the recruitment of circulating immune cells with intestinal tropism. Although the origin of these dysregulations is not currently known, treatments with anti-integrins are already being used successfully (Eksteen *et al*., 2014).

IV.5. Contact with certain infectious agents

Among the infectious agents directly implicated in the etiology of MC, one can mention measles and varicella viruses, as well as Listeria monocytogenes, Candida albicans, invasive Escherichia coli, and especially Mycobacterium avium paratuberculosis (Flemströmand Isenberg *et al*., 2021). The latter, found in unpasteurized milk and drinking water, is implicated due to the presence of tuberculoid granules in cattle, leading to Jones' disease, which shares many similaris with Crohn's disease. Once again, no study has been able to prove the role of an infectious agent, but the discovery of the NOD_2 gene, whose mutation would lead to a defect in bacterial clearance, revives this hypothesis (Bardou *et al*., 2007).

IV.6. Psychological factors

Many patients attribute the origin and progression of their CD to psychosomatic disorders (stress, social problems, mental fatigue). However, establishing a clear link between stress and CD is difficult since studies associating the onset of the disease with stress are retrospective, thus less relevant and heavily biased. In any case, studies mostly indicate an absence of correlation between major life events (such as the death of a loved one) and CD (Lerebours *et al*., 2003; Goodhand *et al*., 2012).

V. Clinical signs of crohn's disease

As the disease can affect all segments of the digestive tract, from the mouth to the anus, clinical manifestations can vary from one person to another. The disease manifests in various ways, through a combination of digestive, general, and extra-digestive symptoms. It should be noted that no symptom is specific to Crohn's disease; other conditions can cause similar manifestations, hence the diagnostic difficulty (Cartign *et al*., 2016; Benrezkallah *et al*., 2017).

V.1. Diarrhea

Diarrhea is present in 90% of cases. It is not typical diarrhea as seen in patients with simpler conditions. In the case of Crohn's disease. Diarrhea is characterized by the presence of blood, pus, or mucus, which is typical of specific lesions in the small intestine and/or colon. Diarrhea can be of different types: Chronic diarrhea (lasting for more than 10 days, characterized by 4 to 8 bowel movements per day and often accompanied by pain), Acute diarrhea (with mucus-blood-streaked emissions and false urges) and Steatorrhea (characterized by abnormally high fat content in the stools, indicating poor absorption in the intestinal tract) (Dominique *et al*., 2012)**.**

V.2. Abdominal pain

This is one of the first symptoms along with diarrhea. It is very common during flare-ups, varying in intensity and often presenting as cramps. These pains often worsen after meals and are generally relieved after defecation. They most commonly occur on the right side, in the iliac fossa, and can simulate acute appendicitis, referred to as pseudo-appendicular syndrome (Bouguen *et al*., 2013)

V.3.Rectal bleeding

This refers to the passage of undigested red blood through the anus independent-ly or mixed with stools (bloody stools), often originating from lesions in the rec-tum. In the case of Crohn's disease, massive rectal bleeding is rare (Almas *et al*., 2017).

V.4. Ano-perineal involvement

Ano-perineal manifestations (Complications)correspond to a rectal syndrome, which is rare due to the usual topography of lesions in Crohn's disease. They can occur regardless of the stage of the disease or the clinical form observed. Ano-perineal lesions are more frequent when Crohn's disease is more distal. They can be divided into pri-mary lesions (fissures, ulcerations) and secondary lesions (strictures, abscesses, and fistulas) (Mouaiz *et al*., 2017).

V.4.1. Anal fissure

Anal fissure is a small, painful wound on the skin of the anus, appearing moist and superficial when newly formed. In the case of a chronic fissure, the wound is deeper with a fibrous base and thickened skin. Anal fissures often mani-fest with chronic constipation or bleeding. According to proctologists, the risk of developing anal fissures increases when Crohn's disease affects the area close to the anus (Denis *et al*., 2018).

V.4.2. Ulceration

These can be considered as a type of anal wound. Digging ulcers are usually located at the anorectal junction. They result in deep tissue loss by erod-ing the underlying tissues until becoming transmural. They are painful to touch and during defecation, especially when affecting the sphincter. Marginal ulcerations, aggressive and extensive, present significant tissue loss starting typically at the anal canal and may extend variably towards the buttocks, scrotum, or vulva. They appear as red-based ulcers with regular borders, exuding, thickened, and extended by suppura-tive detachments, making them particularly debilitating (Dominique *et al*., 2012).

V.4.3. Abscess and fistula

These are the most frequent complications. They result from the deepening of intestinal ulceration, which then extends through the entire thickness of the intestinal wall. A fistula is characterized by the abnormal formation of a connection or tunnel between two organs following the formation of an ab-scess, which eventually opens into neighboring organs. If the abscess is not promptly treated, it may seek to drain either through the skin, forming an external or cutaneous fistula, or through hollow organs such as the digestive tract, bladder, or vagina, forming an internal fistula (Lanteri *et al*., 2019).

V.4.4. Stricture

This refers to a narrowing of the intestine causing mechanical ob-structive or even occlusive complications. As a result, food passes more slowly, which can lead to various symptoms in patients such as difficulty in passing stool, abdominal pain, gas, nausea, and vomiting (Aoun *et al*., 2019).

V.5. Extradigestive manifestations

Extradigestive manifestations of IBD are common; they can precede the onset of digestive manifestations by several months, posing a diagnostic challenge. They are mainly characterized by osteoarticular, cutaneous, hepatobiliary, and hematological involvement. Historically, they refer to immunological manifestations affecting the joints, spine, eyes, skin, and hepatobiliary

tract. The mechanism responsible for extradigestive manifestations remains mysterious. In all cases, they indicate that IBD is not purely a digestive disease but an inflammatory condition involving genetic and environmental factors. While the primary target is the digestive tract, it affects the entire body (Storch *et al*., 2003; Bengtson *et al*., 2009).

VI. Diagnostic Studies

The diagnosis of CD is a clinical one and can be quite difficult given that the presenting symptoms can be insidious and nonspecific. Red flag symptoms that require further evaluation include weight loss, bloody diarrhea, iron deficiency, and night-time awakenings. Similarly, significant family history of IBD, unexplained elevations in the c-reactive protein level, sedimentation rates, or other acute-phase reactants (eg, ferritin and platelets), or low B_{12} should prompt further investigation (Joseph *et al*., 2017).

VI.1. Laboratory testing

Laboratory testing plays a vital role in diagnosing, monitoring, and managing Crohn's disease. Fecal calprotectin is valuable for ruling out Crohn's disease, particularly in cases with equivocal symptoms. Additionally, a comprehensive panel including complete blood count, metabolic panel, pregnancy test, C-reactive protein, erythrocyte sedimentation rate, and stool studies can aid in diagnosis and severity assessment. Monitoring markers like C-reactive protein, fecal calprotectin, and stool lactoferrin can help gauge disease activity, potentially reducing the need for invasive procedures like endoscopy. Regular monitoring of hemoglobin, hematocrit, folate, iron, and vitamin D levels is essential due to common deficiencies and anemia in Crohn's patients. Patients with extensive bowel resection should be screened for vitamin B12 deficiency. Tuberculosis screening is recommended before initiating biologic agents, and periodic blood count, renal, and hepatic function tests are necessary during treatment with certain medications. Therapeutic drug monitoring can provide valuable guidance in treatment decisions (Colombel *et al*., 2017).

VI.2. Endoscopy and imaging

Endoscopy and imaging are essential tools for diagnosing and monitoring Crohn's disease. Endoscopic procedures allow direct visualization of and access to the bowel lumen (Bengtson *et al*., 2009). Direct visualization allows for identification of characteristic lesions, monitoring the success or failure of therapy, and screening for colorectal cancer. Endoscopic procedures (except capsule endoscopy) also allow for biopsy and therapeutic interventions (Siew *et al*., 2012).

Cross-sectional imaging techniques, including computed tomography (CT), magnetic resonance imaging, and ultrasonography, have come to the forefront in the management of Crohn's disease. These techniques are all useful and provide similar accuracy for making the initial diagnosis, monitoring disease activity, and identifying complications (e.g., fistulas, abscesses). They complement endoscopy because they can identify extraluminal pathology and examine the gastrointestinal tract not accessible to endoscopic procedures. If the patient can tolerate the contrast load, CT and magnetic resonance enterography are preferred to standard CT and magnetic resonance imaging protocols. CT studies provide the most consistent results but have the downside of radiation exposure. Magnetic resonance studies have no radiation exposure, but are expensive, may have limited availability, and are more difficult for patients to tolerate. Ultrasonography is readily available and has no radiation exposure, but it is highly operator dependent and can be limited by body habitus. Choosing which modality to pursue depends on the patient's age, pregnancy status, current clinical condition, local expertise, and availability (Rimola *et al*., 2019).

VI.3. Diagnostic Approach

The diagnosis of Crohn's disease results from clinical findings coupled with endoscopic, histologic, radiologic, and/or biochemical testing. History, physical examination, and basic laboratory findings drive the decision to pursue the diagnosis. If the patient has a toxic presentation, standard CT should be the first test. If the patient does not have a fulminant presentation, ileocolonoscopy with biopsy should be the first test, and esophagogastroduodenoscopy should be considered for children. Cross-sectional imaging should follow so that the full extent of disease seen by endoscopy can be determined or to identify disease not visualized by endoscopy. Identifying the complete extent of disease is important for developing a treatment plan. When ileocolonoscopy and cross-sectional imaging are negative and concern for Crohn's disease is still high, capsule endoscopy would be the next step. If this study is negative, it is moderately certain that the disease is not present (Kornbluth *et al*., 2010).

VII. Treatment

The treatment of CD depends on disease severity, location of disease, and subtype of disease (ie, inflammatory, stricturing, or penetrating). We now also attempt to determine who is at risk for aggressive CD and who may require earlier and more aggressive therapies. Risk factors for aggressive disease activity include age of diagnosis less than 30 years, extensive anatomic involvement, perianal disease, deep ulcers, prior surgery, and stricturing and/or penetrating disease. One of the biggest (Veauthier *et al*., 2018).


Verbena officinalis
&
Curcuma Longa

I. Generalities

Early in evolution, humans turned to the resources present in their natural environment for healing. Plants held a significant role that has never diminished, and it is remarkable to note that most of the plants used in therapy today were discovered before the advent of scientific exploration methods (Alinjhad *et al*., 2016).

Chance and careful observation gradually allowed people to learn and discover the soothing, antiseptic, purifying, cardiotonic, and other virtues of plants. Often treated in a simple mannermixed with water through infusion, decoction, maceration, or percolation to extract the active compoundsplants were ingested orally in the form of herbal tea or potion, or applied to wounds in the form of poultice (Blesa *et al*., 2017).

Medicinal plants can sometimes be used as supplements or alternatives to conventional treatments for Crohn's disease, but it's important to note that their effectiveness and safety may vary. Here are some medicinal plants that have been studied for their potential in managing Crohn's disease: Turmeric, Aloe vera, Chamomile, Boswellia, Ginger… (Weinstock *et al*., 2010).

It's important to note that medicinal plants can interact with other medications and may not be suitable for everyone. Before starting any herbal treatment, it's recommended to consult a healthcare professional, especially a doctor or naturopath, for personalized and safe advice.

II. Verbena officinalis

II.1. Presentation of *Verbena officinalis*

Verbenaceae (common vervain) is a well-known medicinal plant with an established position in European, Asian, and North American medicine. The raw material used in both traditional medicine and modern phytotherapy is the verbena herb (De Figueiredo *et al*., 2002).

Verbena officinalis is a perennial subshrub of the Verbena family, reaching a height of 1.50 to 3.00 meters). The stems are angular, ribbed, with straight and branched branches, bearing pale green (Fig. 8), elongated leaves, which are 3 to 7 centimeters long and 1 to 2 centimeters wide, arranged in whorls of three or four on the stems, with very short petioles, rough to the touch. They emit an odor when crushed. The long flowers (Fig. 8), arranged in spikes, have four petals fused at the base into a tube and spread into four bicolored lobes: white on the outer surface and bluish-purple on the inner surface (Cheurfa *et al*., 2015; Pawel Kubica *et al*., 2020).



Fig. 8: Photograph of *Verbena officinalis L* (https://www.journaldesfemmes.fr).

II.2. Systematics of *Verbena officinalis*

The botanical literature reveals a variety of names, including Aloysia triphylla. It takes the systematic position illustrated in the table (Harley *et al*., 2004)

Table I: Taxonomic identification of *Verbena officinalis* (Vervain)(Harley *et al*., 2004).

REIGN	**PLANTEA**
SUPER-DIVISION	Embryophyta
DEVISION	Tracheophyta
CLASSE	Magnoliopsida
ORDRE	Lamiales
SUPERORDRE	Asteranae
FAMILLE	Verbenaceae
GENRE	Verbena
ESPECE	*Verbena officinalis*

II.3. Chemical composition

Verbena officinalishas a rich chemical composition. The main groups of secondary metabolites determining the biological activity profiles of the raw material are iridoid glycosides, including verbenalin (verbenaloside), aucubin (verbenin), and hastatoside, as well as phenylpropanoid glycosides, and caffeic acid derivatives verbascoside (acteoside) and isoverbascoside (isoacteoside), and eukovoside (Rehecho *et al*., 2011).

In addition, numerous flavonoids have been identified in verbena herb extracts, including compounds common in the plant kingdom such as kaempferol, luteolin, and apigenin, and specific flavonoids such as scutellarein and pedalitin. Also, noteworthy is the presence of phenolic acids: chlorogenic, ferulic, protocatechuic, rosmarinic, and dicaffeoylquinic acid derivatives.

Preliminary research conducted by our team regarded the dynamics of accumulation of these metabolite groups during one vegetative cycle. We have proved the maximum content of iridoids, phenylpropanoid glycosides, flavonoids, and phenolic acids in the material harvested at full bloom (zhang *et al*., 2011).

The terpenoid compounds found in the *V. officinalis* herb are monoterpenoids (citral, limonene, cineole, carvone), diterpenoids (carnosol, carnosic acid, rosmanol, isorosmanol), sesquiterpenoids (caryophyllene oxide, α-curcumane), and triterpenoids (ursolic acid and its derivatives) (khan *et al*., 2016).

Phytochemical analyses have shown that methanolic extracts from *V. officinalis* stems contain sterols such as α-sitosterol, β-sitosterol, and daucosterol (zhang *et al*., 2011). The *V. officinalis* herb contains carbohydrates such as galacturonic acid, arabinose, galactose, rhamnose, xylose, mannose, and glucose, as well as large amounts of bioelements, mainly, potassium, phosphorus, calcium, magnesium, zinc, iron, manganese, and copper (Rehecho *et al*., 2011).

II.4. Traditional use

V. officinalis herb extracts have long been used in traditional medicine. Possible therapeutic applications based on centuries of use of this raw material are confirmed by modern scientific research on the chemical composition and action of active compounds (Rehecho *et al*., 2011).

The *V. officinalis* herb is used as an antimicrobial, secretolytic, and expectorant raw material. *V. officinalis* is used in the treatment of upper respiratory tract diseases, mainly, in inflammation of the throat and sinuses, and in cases of cold, fever, tightness of the chest, bronchitis, asthma, pertussis, and sinusitis (Schönbichler*et al*., 2013).

Extracts from *V. officinalis* leaves are also known to help in the treatment of urinary tract disorders, such as urinary stones and urinary tract infections, and also have a diuretic effect. In women, the raw material is used to treat menstrual disorders, and in nursing mothers, to stimulate lactation V. officinalis has been successfully applied in disorders of the nervous system such as depression, insomnia, stress, anxiety, chronic fatigue syndrome, nervous exhaustion, sexual neurosis, and headache (khan *et al*., 2016).

V. officinalis is also used in the treatment of digestive tract disorders, such as abdominal colic, jaundice, gallbladder inflammation, diarrhea, dysentery, stomachache, and intestinal worms (Enyaw*et al*., 2014). Extracts from the *V. officinalis* herb are used to fight fever accompanying colds; they also have supportive properties in the treatment of malaria and rheumatism.In skin

diseases, the *V. officinalis* herb is used as a softening, anti-inflammatory, and antibacterial agent, among others, in the treatment of difficult healing wounds and in gingivitis (khan *et al*., 2016). Moreover, V. officinalis extracts can be used topically in cases of wounds, bites, oral and throat inflammation, and muscle spasms (Speroni *et al*., 2007).

II.5. Biological Activity of Extracts and Components Responsible

In this study, we will highlight the most significant activities of the plant while considering its anti-inflammatory and analgesic activities.Phenolic compounds (mainly flavonoids, phenolic acids, and phenylpropanoids) are believed to be responsible for most of the pharmacological activities of common vervain such as analgesic, anti-inflammatory, and antioxidant effects (Quirantes-Pin*et al*., 2009).

II.5.1. Antioxidant effect

Verbena possesses several therapeutic virtues and biological activities. Several categories of phytochemical compounds have been identified in its various parts such as terpenes, phenylpropanoids, phenylethanoids, flavonoids, and phenolic compounds. These confer bioactive potential to the plants (Touati *et al*., 2021). Moreover, the infusion exhibits strong superoxide radical scavenging activity and moderate activity against hydroxyl radical and hypochlorous acid (Bekara*et al*., 2020). Extracts from common verbena leaves have significant antioxidant activity attributed to the presence of phenolic compounds, flavonoids, terpenes, phenylpropanoids, and phenylethanoids (Cheurfa and Allem, 2015).

II.5.2. Anti-inflammatory activity

V. Officinalis is a medicinal plant containing several phenolic compounds (polyphenols and flavonoids), and its leaves exhibit aromatic, antispasmodic, antipyretic, sedative, and digestive properties (Kaskoos, 2019). Phenolic compounds are believed to be responsible for most of the pharmacological activities of verbena, such as analgesic, anti-inflammatory, and antioxidant effects (Lima *et al*., 2020). *V Officinalis* contains high levels of propanoid polyphenols that inhibit the expression of various pro-inflammatory cytokines. Furthermore, verbena improves the inflammatory process and vascular dysfunction associated with this condition, mediated by phenolic compounds, notably verbascoside and other glycosylated phenylpropanoids (Miraj *et al*., 2016).

The analgesic efficacy of lemon verbena, on the other hand, helps alleviate mild pains and contributes to its use in cases of mild to moderate headaches or migraines.Externally applied, in the form of compresses or in aromatic baths, lemon verbena essential oil can provide targeted

relief, while internally, an infusion of lemon verbena leaves helps combat inflammation more generally(Mashayekhi-sardoo *et al*., 2020).Given these properties, lemon verbena proves to be a natural remedy of first choice for those seeking to alleviate discomfort associated with inflammation and pain without resorting to synthetic medications. Moreover, *V. officinalis* extracts could be used topically in cases of wounds, bites, oral and throat inflammation, muscle spasms, and rheumatic conditions(Virginie Missiaen *et al*., 2024).

II.5.3. Properties of stomachic, carminative, and antispasmodic

On the digestive level, verbena acts effectively due to its stomachic properties which promote good digestion. It stimulates bile secretion, thus aiding in the breakdown of fats and reducing feelings of heaviness after meals. As a carminative, it also helps expel intestinal gas, reducing bloating, flatulence, and digestive discomfort(Virginie Missiaen *et al*., 2024).

Its antispasmodic effects are beneficial in relaxing the smooth muscles of the digestive system, thereby relieving intestinal spasms and gastralgia that may occur due to inadequate diet or nervous tension. This property also makes it an ally against menstrual pains, where it acts by relaxing the uterus (Miraj *et al*., 2016).

The proven, very rich and diverse chemical composition of the raw material (iridoids, phenylpropanoid glycosides, flavonoids, terpenoids, phenolic acids, the presence of essential oil) determines its valuable therapeutic properties. Nowadays, officially, the *V. officinalis* herb is recommended in the treatment of the digestive tract disorders such as abdominal colic, jaundice, gallbladder inflammation, and intestinal worms, and urinary tract disorders such as urinary stones, urinary tract infections, and reproductive system diseases, e.g. dysmenorrhea (Lima *et al*., 2020).

In infusion, essential oil, or other suitable forms, it thus proves to be a real asset for maintaining general well-being and for specifically treating ailments related to the digestive system and stress(Virginie Missiaen *et al*., 2024).

III. *Curcuma Longa*

III.1. Presentation of *Curcuma Longa*

Curcuma longa L. (Zingiberaceae) is a perennial herb widely cultivated in tropical regions of Asia.Perennial herb reaching up to 1.0m in height; its stout, fleshy main rhizome is nearly ovoid, measuring about 3cm in diameter and 4cm in length. Lateral rhizomes are slightly bent, ranging from 1cm to 2–6cm in length, and flesh orange in color. The large lanceolate leaves are uniformly green, reaching up to 50cm in length and 7–25cm in width, with an acute and caudate apex and tapering base. Petioles and sheaths are sparsely to densely pubescent (Hermman *et al*., 1990). The apical spike is cylindrical, measuring 10–15cm in length and 5–7cm in diameter. Bracts are white or white with a light green upper half, about 5–6cm long, each subtending flower, with bracteoles up to 3.5cm long (Fig. 9). Pale yellow flowers are approximately 5cm long; the calyx is tubular, unilaterally split, and unequally toothed, while the corolla is white, with a funnel-shaped tube and a 3-lobed limb. Stamens are lateral, petaloid, and widely elliptical, longer than the anther; the filament is united to the anther around the middle of the pollen sac, spurred at the base. The ovary is trilocular, and the style is glabrous. The capsule is ellipsoid, and the rhizomes are orange within (Keita *et al*., 1996).

III.2. Systematics of *Curcuma longa L*.

The botanical literature reveals a variety of names. It takes the systematic position illustrated in the table II (Sayantani, 2019).

Fig. 9: Photograph of *Curcuma longa L*. (https://fr.wikipedia.org/wiki/Curcuma#).

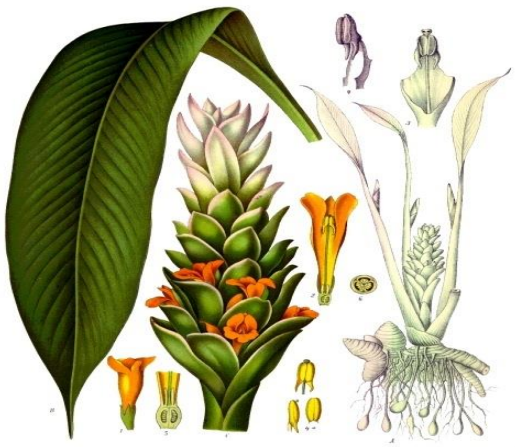


Table II: Taxonomic identification of *Curcuma longa L*. (Sayantani,2019).

REIGN	**PLANTEA**
SUPER-DIVISION	Spermatophyta
DEVISION	Magnoliophyta
CLASSE	Zingiberidae
ORDRE	Zingiberales
FAMILLE	Zingiberaceae
GENRE	Curcuma
ESPECE	Curcuma longa

III.3. Chemical composition

The major constituent, curcumin (diferuloylmethane) is the most important fraction of Curcuma longa. It melts at 176-177°C and forms red-brown salts with alkalis. Curcumin is soluble in ethanol, alkalis, ketones, acetic acid, and chloroform; however, it is insoluble in water. In the molecule of curcumin, the main chain is aliphatic and unsaturated, and the aryl group can be substituted or not. Its main components are curcumin (60%), desmethoxycurcumin, monodemethoxycurcumin, bisdemethoxycurcumin, dihydrocurcumin, and cyclocurcumin. Curcumin's oxidation yields vanillin (Kavirayani, 2014). The essential oil (5.8%) obtained by steam distillation of rhizomes contains α-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%), and sesquiterpenes (53%). Curcumin (diferuloylmethane) (3–4%) is responsible for the yellow color and comprises curcumin I (94%), curcumin II (6%), and curcumin III (0.3%). Demethoxy and bisdemethoxy derivatives of curcumin have also been isolated (Gupta *et al*., 2010).

III.4. Challenges and Metabolism in the Body

Curcumin, despite its therapeutic potential, faces significant hurdles due to its low solubility in water and rapid degradation in alkaline environments within the digestive tract. These challenges impede its absorption, with only a small fraction making it into the bloodstream (Liu, 2016). Upon absorption, curcumin undergoes rapid metabolism, predominantly in the liver, resulting in various metabolites. These metabolites, more water-soluble than curcumin itself, are then distributed throughout the body, targeting no specific organ (Nelson *et al*., 2017).

Metabolic reactions include phase 1 and phase 2 processes, involving reduction of double bonds and conjugation with glucuronide or sulfate groups, respectively. These reactions enhance water solubility, facilitating elimination via urine or feces within 24 to 48 hours (Vareed *et al*., 2008).

Despite the limited bioavailability of curcumin, its journey through the body underscores its potential as a therapeutic agent, albeit with considerations for its metabolic fate and elimination pathways (Liu, 2016).

III.5. Traditional use

Curcuma species are used in Asian countries like Bangladesh, Malaysia, India, Nepal, and Thailand for treating pneumonia, bronchial complaints, leucorrhoea, diarrhoea, dysentery, infectious wounds or abscesses and insect bites. Primordial and current medicinal practices in India utilize Turmeric to treat jaundice, rheumatism, cough and several disorders. Emphasizing curcumin's maximal ethnomedicinal efficiency in India, Vaughn reported its use in treating obesity and inflammation. In Pakistan, powdered C. longa extract is used in curing pimples and wounds. An ethnomedicinal survey in Nepal by Singh and his collaborators (2018) reported that paste derived from the rhizome of C. longa could be applied to treat wounds and injuries. The juice from its leave has an anthelmintic effect and serves as a blood purifier. The juice obtained from powdered C. longa is also utilized in the Philippines for the treatment of Arthritis.

In the Kurdish community of Iraq, leaves from C. longa are used in facial massages and the treatment of Arthritis. At the same time, the decoction obtained from the rhizome has been reported for its anticancer activity. In Korea, Kim and Song (2014). have also stated its usage in treating gastroenteric disorders. Merzoukiand his collaborators (2022) reported that the oral intake of C. longa powder aids digestion and could serve as a calefacient and also reported using extracts from the rhizome as a condiment for cooking in Morocco. An extensive ethnoveterinary survey in Trinidad and Tobago, as reported, revealed the diverse therapeutic efficacy of different parts of C. longa on horses. The survey reported how the rhizomes from C. longa were pounded and used in treating horses' hoofs and how the powder from the plant's rhizome was used to treat Arthritis. In Colombia, the plant is used to treat diabetes, obesity, prevent indigestion, and thrombosis, amongst several therapeutic activities. Curcumin derived from the rhizomes of C. longa has been identified as an ancient remedy to a broad spectrum of diseases and is also utilized by diverse communities, most notably the Asian community, with applications dating back over 2500 years (Emeka *et al*., 2023).

III.6. Biological Activity of Extracts and Components Responsible

Curcumin is the major compound found in turmeric rhizome and the most studied. It exhibits antiparasitic, antispasmodic, anticarcinogenic, and gastrointestinal effects whereas it shows antiparasitic and anti-inflammatory activity. It also has antidiabetic, antimutagenic, anticoagulant, antioxidant, an-tiviral, antiprotozoal, antiulcer, antifungal, and hypercholesteremic properties (Kumari and Subramanya, 2020; Sivakumar *et al*., 2022).

III.6.1 Gastrointestinal effects

Turmeric has a significant impact on the digestive system. Curcumin's anti-inflammatory effects and therapeutic advantages have been established with gastritis, Helicobacter pylori disease, stomach ulcers, inflammatory bowel disease, crohn's disease, and ulcerative colitis. In rats exposed to various gastrointestinal shocks, it reduces ulcer development induced by anxiety, alcohol, indomethacin, reserpine, pyloric ligation, and increased stomach wall mucus. It also reduces gastrointestinal contractions and boosts the release of bicarbonate, gastrin, secretin, and pancreatic enzymes (Sivakumar *et al*., 2022).

III.6.2. Anti-inflammatory activity

Research shows curcumin is a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation. Curcumin modulates the inflammatory response by down-regulating the activity of cyclooxygenase-2 (COX-2), lipoxygenase, and inducible nitric oxide synthase (iNOS) enzymes; inhibits the production of the inflammatory cytokines tumor necrosis factor-alpha (TNF-a), interleukin (IL) -1, -2, -6, -8, and -12, monocyte chemoattractant protein (MCP), and migration inhibitory protein; and down-regulates mitogen-activated and Janus kinases (Foudi *et al*., 2009; Shaikh and Prabhakar, 2020).

COX-2 and iNOS inhibition are likely accomplished via curcumin's suppression of nuclear factorkappa B (NF-κB) activation. NF-κB, a ubiquitous eukaryotic transcription factor, is involved in regulation of inflammation, cellular proliferation, transformation, and tumorigenesis. Curcumin is thought to suppress NF-κB activation and proinflammatory gene expression by blocking phosphorylation of inhibitory factor I-kappa B kinase (Shaikh and Prabhakar, 2020). Suppression of NF-κB activation subsequently down-regulates COX-2 and iNOS expression, inhibiting the inflammatory process and tumorigenesis. In an animal model of inflammation, curcumin also inhibited arachidonic acid metabolism and inflammation in mouse skin epidermis via downregulation of the cyclooxygenase and lipoxygenase pathways (Foudi *et al*., 2009).

Curcumin's inhibition of inflammatory cytokines is achieved through a number of mechanisms. In vitro studies indicate curcumin regulates activation of certain transcription factors such as activating protein-1 (AP-1) and NF-κB in stimulated monocytes and alveolar macrophages, thereby blocking expression of cytokine gene expression. Down-regulation of intercellular signaling proteins, such as protein kinase C, may be another way in which curcumin inhibits cytokine production (Julie,2009).

Methodological framework of the field study

I. Methodology and procedures of the field study

Conducting a scientific study necessitates identifying a suitable methodology, ensuring its robustness, and employing appropriate tools to achieve its objectives effectively. This study aims to elucidate its adopted methodology and the specific data collection tools utilized to meet its goals.

I.1. Methodology

The methodology used in this research is foundational to any scientific inquiry. This field study begins by collecting data on the study topic through distributing a questionnaire designed specifically for this research. Subsequently, a variety of statistical methods are applied to analyze the quiz results, which serve as a critical tool for drawing conclusions based on the gathered data. Finally, conclusions are drawn and hypotheses are tested by interpreting the quantitative results obtained using the SPSS software program.

I.2. Methods and techniques for data collection

To tackle the issues pertinent to this study, the analytical aspects of the study topic were addressed through the collection of primary data using a questionnaire tool. The quiz served as the primary means of gathering data, consisting of a series of questions or statements for respondents to answer. It included a specific set of statements aligned with the study's objectives and inquiries. Respondents provided their answers using a five-point Likert scale, where each response carried relative importance. In addition to these statements, the quiz also included supplementary questions.

The quiz was instrumental in gathering essential data for the study through the following steps: identifying the main dimensions of the questionnaire, ensuring clarity of all statements and questions to facilitate understanding and analysis, finalizing the quiz in its completed form, and distributing and presenting it to the herbalists. These steps delineate the systematic approach used to leverage the quiz for data collection in this study.

Personal interviews were relied upon (with the difficulty of conducting face-to-face interviews), which is considered one of the most important means of collecting data, to enhance the results of the quiz and ensure the accuracy of the results for this study. This method was used during the distribution of quiz in order to ensure the best possible answers to the quiz distributed.

II. QUIZ

Quizzes for Crohn’s Diseease patients

The researchers are conducting a study titled "The Contribution of Pharmaceuticals and Herbs in Improving or Treating Symptoms of Crohn's Disease" as part of the requirements for obtaining a Master's degree in Life and Natural Sciences, specializing in Biochemistry at the University of Setif-1. The questionnaire is specifically designed for individuals experiencing symptoms of Crohn's disease. Your responses are crucial for this scientific research and will be treated with complete confidentiality.

Please respond to all sections of the quiz objectively, as the accuracy of the results heavily relies on your answers.

Thank you in advance for your time and cooperation.

Researcher: Ghedjati Thamar
Phone:…….
Email:……..

Researcher: Boucetta Racha Sofia
Phone:…….
Email:……..

General information about the patient

How old are you (years)?
- (1-14) ☐ - (15-30) ☐ - (30-50) ☐
- (50-70) ☐ -Over 70 ☐

What is your gender?
- Male ☐ - Female ☐

Where is your Crohn's disease located?
- Terminal ileum ☐ - Ileal with colon ☐
- Terminal ileum and colon ☐ - Colon ☐
Other location ……

What treatments have you used?
- Medical ☐ Herbal ☐ - Both ☐
-Other method…….

Symptoms of Crohn's disease and its causes

What do you believe are the causes of your illness?
- Psychological factors ☐ - Dietary reasons ☐
- Lifestyle ☐ - Genetic factors ☐
- Bacterial or viral causes, etc. ☐
Other reasons……..

Is any relative affected by this disease?
- Yes ☐ - No ☐
- I don't know ☐

What symptoms do you have during a relapse?
Abdominal pain and cramping ☐ - Diarrhea ☐
Constipation ☐ - Rectal bleeding ☐
- Shortness of breath ☐ - Fistulas ☐
- Blood clots ☐ - Mouth ulcers ☐ - Rectal issues ☐
- Kidney problems ☐ - Inability to control gas ☐
- Weight loss ☐ - Digestive disorders ☐
- Rapid heartbeat ☐ - Body aches ☐
- Fatigue and tiredness ☐ - Skin problems ☐
- Osteoporosis ☐ Nausea or vomiting ☐
Other symptoms.....

Which of these foods cause harm to you?
- Milk and dairy products ☐ - Eggs ☐
- Fats ☐ - Gluten and wheat protein ☐
- Fiber ☐ - Spices ☐ - Raw vegetables ☐
- Caffeine and stimulants ☐
..... Other food -

Methods of Treatment

First : treatmentwithmedications

What medications have you previously use?
Prednisolone-Méthotrexate ☐
Azathioprine-InfleximabAspirine ☐
Adalimumab-Vedolizumab ☐
Outher……

What side effects have you noticed
-Nausea ☐ Diarrhea ☐
-Abdominal painLever ☐ Inflammation ☐
Headache ☐ -Vomitin ☐
Osteoporosis ☐

Have you noticed an improvement when using these medications?
–Yes ☐ -No ☐

Have you noticed side effects when taking these medications?
-Yes ☐ -No ☐

Second : Herbaltreatment

What herbs did you use for treatment?	**Agree**	**Stronglyagree**	**Disagree**	**No opinion**
Turmeric				
Aloe vera				
Ginger				
Siberian ginseng				
Chamomile				
Oakbark				
Teucriumpolium				
Frankincense				
Pomegranate				
Necessitypaper				
Aloysiacitriodora				
Other herbs	……			

If yes, mention the herb that helps you the most ……

Have you noticed an improvement when using herbs?
-Yes ☐ -No ☐

Do you prefer medication:
With herbs ☐ - Medicines ☐ - Other methods ☐

Have you noticed side effects when consuming herbs:
-Yes ☐ -No ☐

III. Statistical methods related to the study

After gathering the final number of accepted questionnaires, the researcher utilized various essential statistical methods to analyze the data, aiming to test hypotheses, derive results, and formulate recommendations. The analysis was conducted using the Statistical Package for the Social Sciences (SPSS), a widely acknowledged statistical software.

Specifically, descriptive and inferential statistical analyses were employed to obtain comprehensive indicators of the study population's characteristics and to describe the variables under study. This approach facilitated effective interpretation and presentation of the data, thereby supporting the study's findings and conclusions.

The study employed several descriptive statistical methods to analyze the data comprehensively. Frequency distributions were used to illustrate the distribution of responses across each questionnaire item. Percentages were calculated to determine the proportion of herbalists' responses to key statements on the axes, presented as percentages. Mean values were calculated to gauge the average response of the study sample to each questionnaire statement, offering insights into the degree of agreement or disagreement among respondents. Standard deviation measurements were used to assess the dispersion of responses around their respective means; a lower standard deviation indicated responses clustered closely around the mean. These statistical approaches were instrumental in analyzing data, understanding sample perspectives, and interpreting the study's results accurately and logically.

Result and discussion

I.General information about the patient

I.1. Gender

According to studies and data, 58% of individuals affected by Crohn's disease are women, while men comprise 42% (Fig. 10). This suggests a higher susceptibility among women compared to men. Several factors contribute to this gender difference, including hormonal interactions, genetics, and environmental influences. It's worth noting that while significant, this gender gap can vary among different studies.

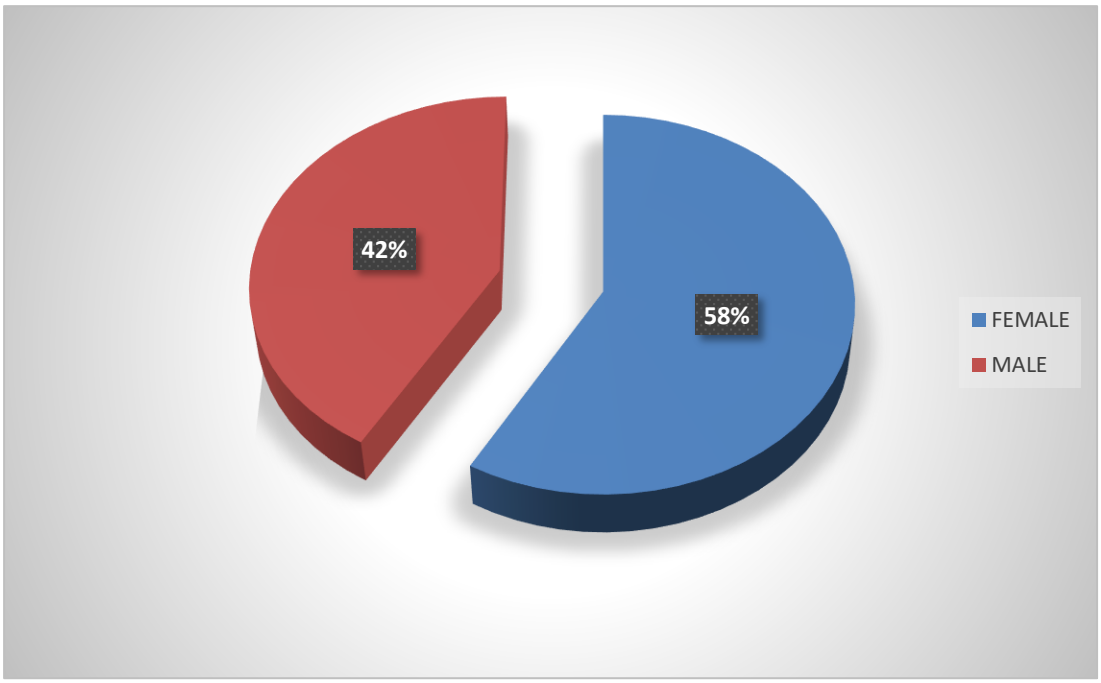


Fig. 10: Gender individuals affected by Crohn's disease

I.2. Old individuals affected by Crohn's disease

Crohn's disease is most prevalent among individuals aged 15 to 30 years, comprising the majority of diagnosed cases. This age group undergoes significant biological and emotional changes, potentially amplifying both the onset and detection of the disease.

Conversely, younger individuals aged 1 to 14 years exhibit lower susceptibility to Crohn's disease, with fewer reported cases.

The highest vulnerability occurs within the 15 to 30 age range, encompassing approximately 75% of diagnosed cases. This demographic faces various environmental and lifestyle factors that may contribute to the increased prevalence (Fig11).

As individuals enter adulthood (ages 30 to 50 years), the incidence of Crohn's disease decreases, accounting for around 25% of reported cases in this age bracket (Fig11).

Elderly individuals (ages 50 to 70 years) are less frequently affected by Crohn's disease, experiencing a lower incidence rate compared to younger age groups.

Overall, while Crohn's disease most commonly manifests during adolescence and early adulthood, it can occur at any age. However, its prevalence generally decreases as individuals move into older age groups.

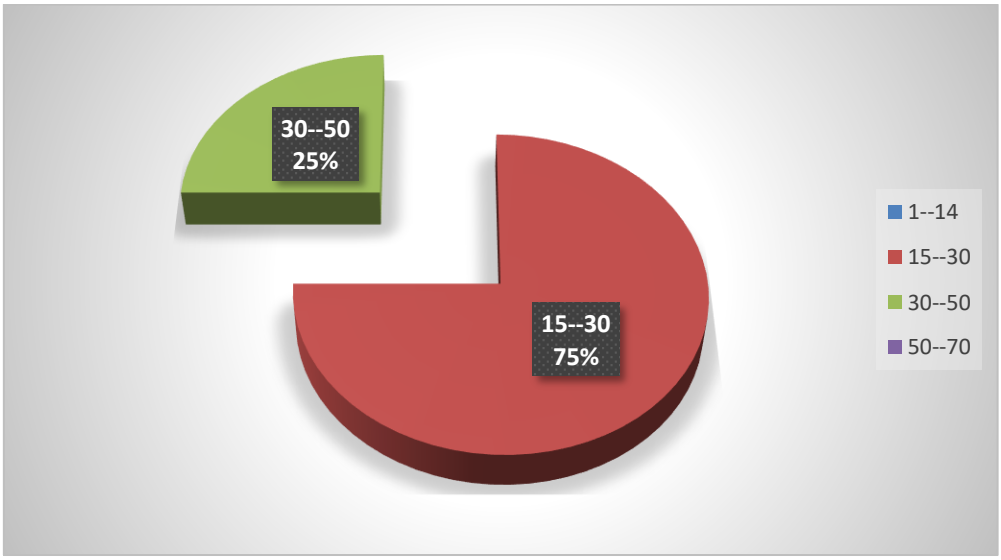


Fig. 11: Old individuals affected by Crohn's disease

I.3. Treatments used

A considerable number of patients (37.4%) opt for medication therapy, indicating their confidence in prescribed medications recommended by healthcare professionals, known for their efficacy in managing the disease. Conversely, a smaller fraction (4.2%) prefers herbal or plant-based treatments, signaling a growing interest in alternative and natural approaches (Fig12).

Significantly, a majority of patients (58.3%) adopt a combined approach, integrating prescribed medications with herbal remedies. This dual strategy may indicate a willingness to explore diverse therapeutic options, aiming to enhance symptom relief and improve overall quality of life.

The diversity in treatment preferences highlights the importance of personalized care in Crohn's disease management, taking into consideration individual choices, severity of symptoms, and treatment responses. It is essential for patients to receive comprehensive information and regular

medical monitoring to make informed decisions about their treatment and effectively manage their health condition.

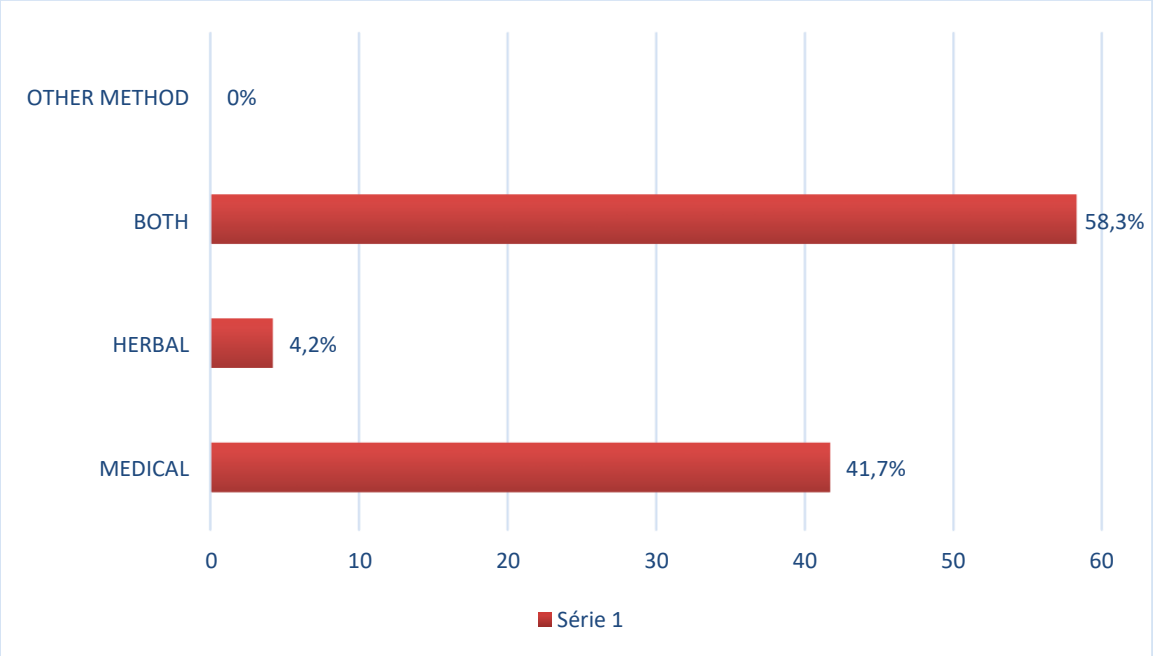


Fig. 12: Treatments used

I.4. Location of Crohn's disease

Among the 25 cases of Crohn's disease patients, the distribution of affected areas offers valuable insights into the disease's impact on different parts of the digestive system (Fig.13).

Firstly, 45.5% of cases show inflammation in the terminal ileum, where the small intestine connects to the colon. This high prevalence suggests that terminal ileum involvement is a prominent feature of Crohn's disease (Fig.13).

6.1% of cases exhibit inflammation in both the terminal ileum and the colon, indicating a more widespread disease within the digestive tract. This dual-site involvement often correlates with more severe symptoms and complications (Fig.13).

20.2% of cases involve both the ileum and the colon, highlighting inflammation that spans across both sections of the intestine. Such cases pose challenges in management due to the complex nature of symptoms and treatment options.

10.6% of cases are affected in the colon alone, indicating that while less common than terminal ileum involvement, colonic inflammation remains significant in Crohn's disease.

Finally, 4 (18%) cases involve other locations such as the mouth and esophagus, stomach and duodenum, and the anus and rectum. These instances underscore the disease's potential to affect various parts of the digestive system beyond the intestines, albeit rarely. Management of these cases often requires specialized approaches tailored to the affected area.

In summary, the distribution of affected areas in Crohn's disease patients illustrates the condition's diverse nature, with varying extents of involvement across different parts of the digestive tract. This complexity emphasizes the importance of personalized treatment strategies that address each patient's specific disease manifestations and requirements.

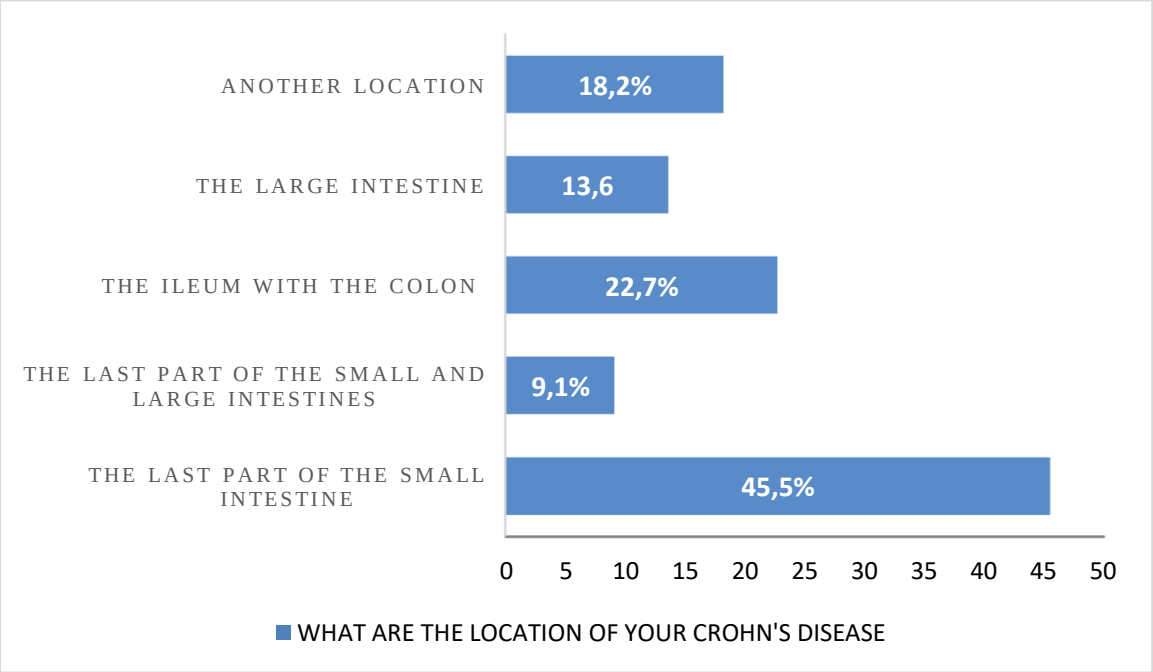


Fig. 13: Location of Crohn's disease

II. Symptoms of Crohn's disease and its causes

II.1. Relatives being infected with this disease

During our interviews, we queried patients about any family history of Crohn's disease to gauge the influence of genetic factors on its development. Of those queried, 79.2% responded that none of their relatives had been diagnosed with the disease, while 12.5% confirmed a family member's diagnosis (Fig.14).

It's essential to clarify that Crohn's disease is not strictly hereditary in the conventional sense, where it passes directly from parents to children. However, it does demonstrate a familial tendency, indicating a genetic role in increasing susceptibility. Individuals with affected family members are at a heightened risk of developing the disease. Research has identified several genes associated

with an increased susceptibility to Crohn's disease, particularly those involved in immune system functions.

Nevertheless, it's crucial to recognize that genetics alone do not determine Crohn's disease. Environmental factors such as diet, smoking, and disruptions in the gut microbiome also contribute significantly. These environmental influences can interact with genetic predispositions, further influencing disease development. Therefore, Crohn's disease is understood as a complex interplay between genetic and environmental factors.

In summary, while genetics contribute to the risk of Crohn's disease, environmental and other biological factors are equally important. This multifaceted interaction underscores the complexity of the disease and emphasizes the need for a comprehensive approach to understanding its impact and treatment.

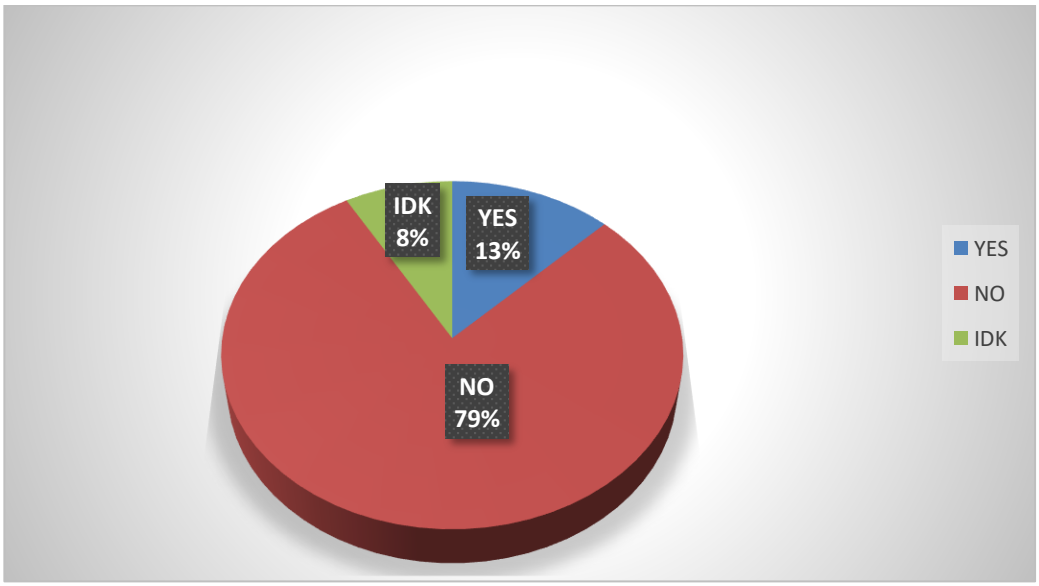


Fig.14: Relatives being infected with this disease

II.2. Causes of illness

Patients with Crohn's disease hold varied beliefs about the causes of their condition (Fig. 15):

- **66.7% believe in psychological causes**: Many patients attribute stress, anxiety, and psychological pressure to exacerbating symptoms and possibly triggering the onset of the disease. Psychological factors are thought to impact the immune system, potentially increasing inflammation in the digestive tract.
- **37.5% believe in dietary causes**: This group links their disease to the types of food they consume. Certain foods may irritate the intestines or provoke inflammation. An

imbalanced diet or consumption of heavily processed foods are considered contributing factors.

- **12.5% believe in lifestyle causes**: Factors such as lack of physical activity, smoking, and alcohol consumption are seen as potential contributors. These lifestyle choices can negatively affect overall health and may increase the risk of developing or worsening Crohn's disease symptoms.
- **20.8% believe in genetic causes**: Patients in this category acknowledge the role of genetics in Crohn's disease, particularly if there is a family history of the condition. Genetic factors may predispose some individuals to be more susceptible.
- **33.3% believe in viral or bacterial causes**: These patients consider infections caused by viruses or bacteria as potential reasons for Crohn's disease. Changes in the gut microbiome or exposure to specific infections might trigger an abnormal immune response, leading to the development of the disease.

These percentages illustrate the diverse beliefs among patients regarding the potential causes of Crohn's disease. It shows that many patients perceive psychological and dietary factors as particularly influential on their health condition. Understanding these varied perspectives is crucial for tailoring treatment approaches and providing comprehensive care to patients with Crohn's disease.

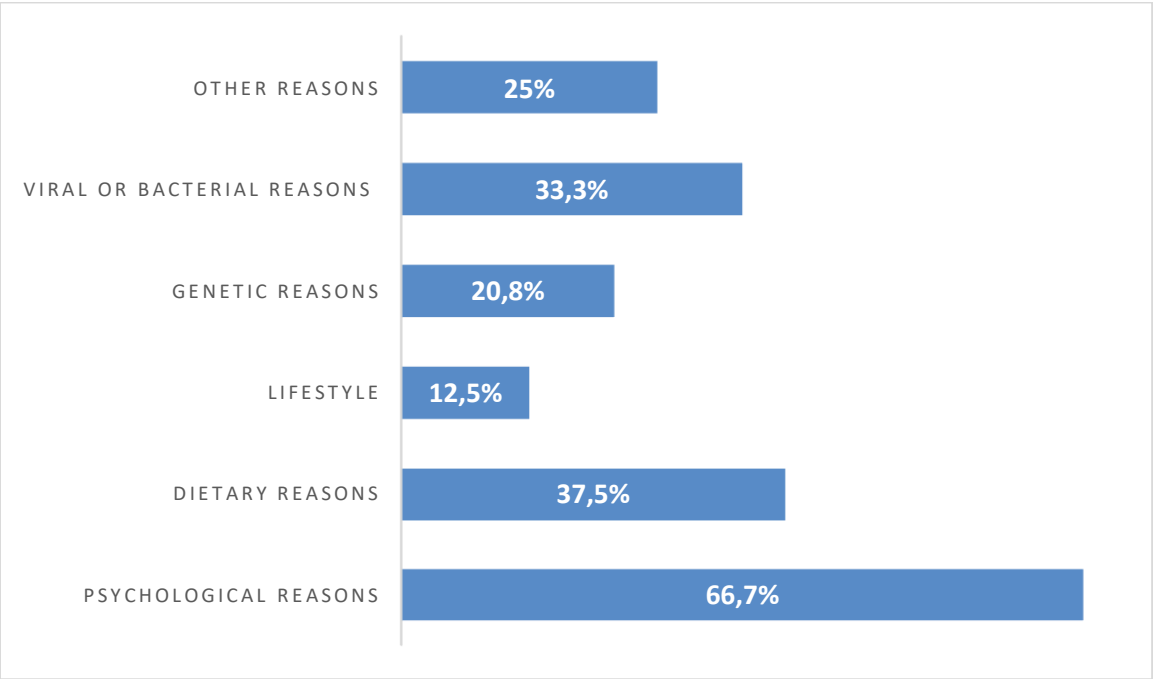


Fig. 15: Causes of illness

II.3. Symptoms during a relapse

A high percentage of patients with Crohn's disease experience symptoms that significantly affect their daily lives (Fig.16):

- **Abdominal pain and intestinal cramps (91.7%):** These symptoms are prevalent and can cause considerable discomfort, impacting quality of life.
- **Continuous diarrhea (62.5%)**: Indicates severe disruption in intestinal function and digestion.
- **Presence of blood in the stool (37.5%)**: Suggests potential gastrointestinal issues, such as inflammation or other serious conditions.
- **Fatigue and fever (66.7%):** Signs that the body is responding to illness, possibly indicating inflammation or infection.
- **Appetite loss and weight loss (70.8%)**: Highlight the disease's impact on the digestive system and the body's ability to absorb nutrients.

The simultaneous occurrence of these symptoms suggests that Crohn's disease can be severe and have a comprehensive impact on the body. These symptoms can indicate various medical conditions, including inflammatory diseases, infectious diseases such as viral or bacterial infections, or more serious conditions like cancer. Therefore, it is crucial for individuals experiencing these symptoms to seek medical attention promptly for an accurate diagnosis and the development of an appropriate treatment plan.

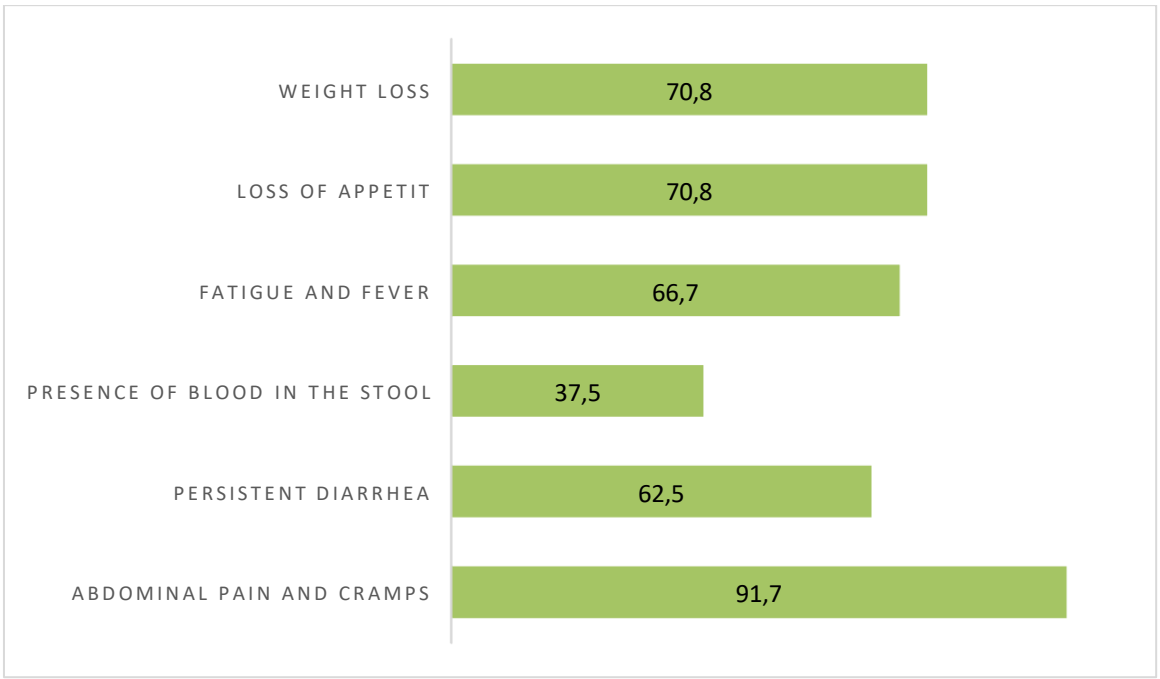


Fig. 16: Symptoms during a relapse

During a relapse of Crohn's disease, patients may experience several symptoms, including (Fig.17):

1. **Abdominal pain and cramps (70.8%)**: Common symptoms during flare-ups, varying in severity.
2. **Diarrhea and digestive disturbances (41.7%)**: Indicates worsening intestinal inflammation, causing significant discomfort.
3. **Intestinal bleeding and shortness of breath (12.5%)**: Bleeding suggests severe inflammation or damage in the digestive tract; shortness of breath may indicate pulmonary complications.
4. **Nausea and vomiting (45.8%)**: Result from gastric irritation and stress due to intestinal obstructions.
5. **Fistulas and rectal problems (37.5%)**: Fistulas are serious complications causing pain and infections; rectal problems may include fissures or inflammations.
6. **Mouth ulcers (41.7%)**: Due to systemic inflammation associated with Crohn's disease.
7. **Weight loss (33.3%)**: Resulting from decreased appetite, digestive disturbances, and malabsorption of nutrients.
8. **Body pains (20.8%)**: From generalized inflammation and immune response.
9. **Fatigue and exhaustion (50%)**: Common due to disease-related inflammation and psychological stress.

These complex and varied symptoms highlight the importance of careful management and regular medical follow-up for Crohn's disease patients to prevent complications and improve their quality of life.

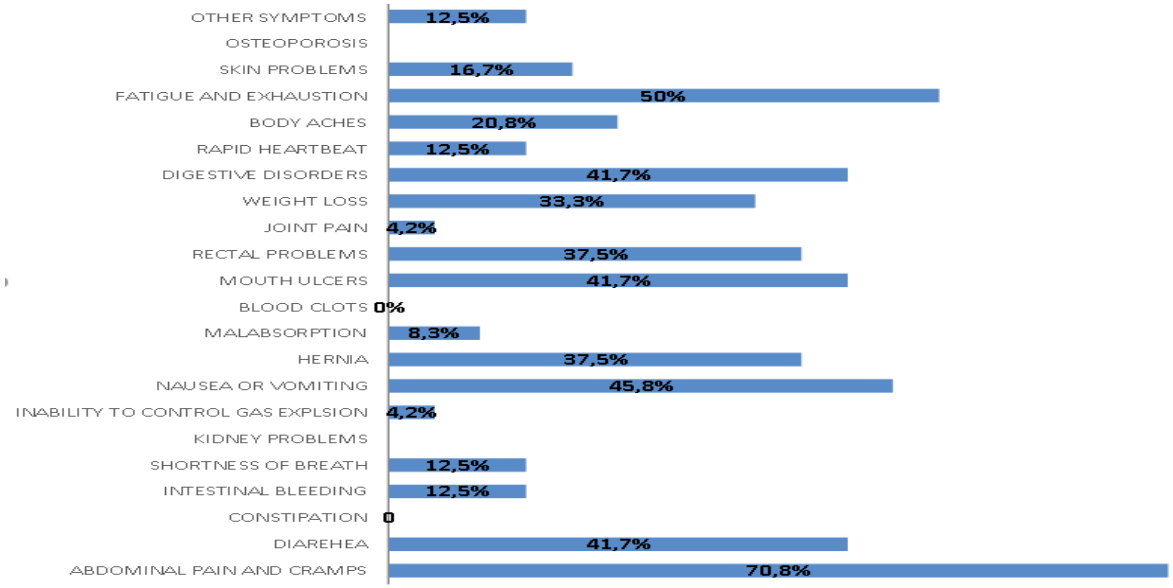


Fig. 17: Varied symptoms for Crohn's disease patients

II.4. Foods that cause harm

Based on the results, it appears that certain foods may exacerbate symptoms for Crohn's disease patients. Here's a detailedanalysis of the findings (Fig.18) :

1. **Milk and dairy products, as well as raw vegetables**: 38.1% of participants believe that consuming milk and dairy products, along with raw vegetables, may worsen symptoms. This underscores the importance of avoiding lactose-containing foods and reducing intake of raw vegetables for some patients.
2. **Fats and spices**: 57.1% of participants believe that consuming fats and spices can aggravate symptoms. Patients should avoid fatty foods and spicy spices to reduce irritation.
3. **Caffeine and stimulants**: 47.6% of participants noted that caffeine and stimulants may increase symptoms. Patients should be cautious with caffeinated beverages such as coffee and soft drinks.
4. **Fiber**: 23.8% of participants believe that fiber may exacerbate symptoms, potentially increasing irritation and diarrhea in some patients.
5. **Eggs, protein, and gluten**: 19% of participants believe that consuming eggs, protein, and gluten may worsen symptoms, possibly due to sensitivity to these components.

It's important to note that individual responses to foods can vary among Crohn's disease patients. Therefore, each patient should carefully experiment with different foods and monitor their reactions to determine which ones negatively affect their condition. This personalized approach is crucial in managing dietary triggers and improving overall symptom management in Crohn's disease.

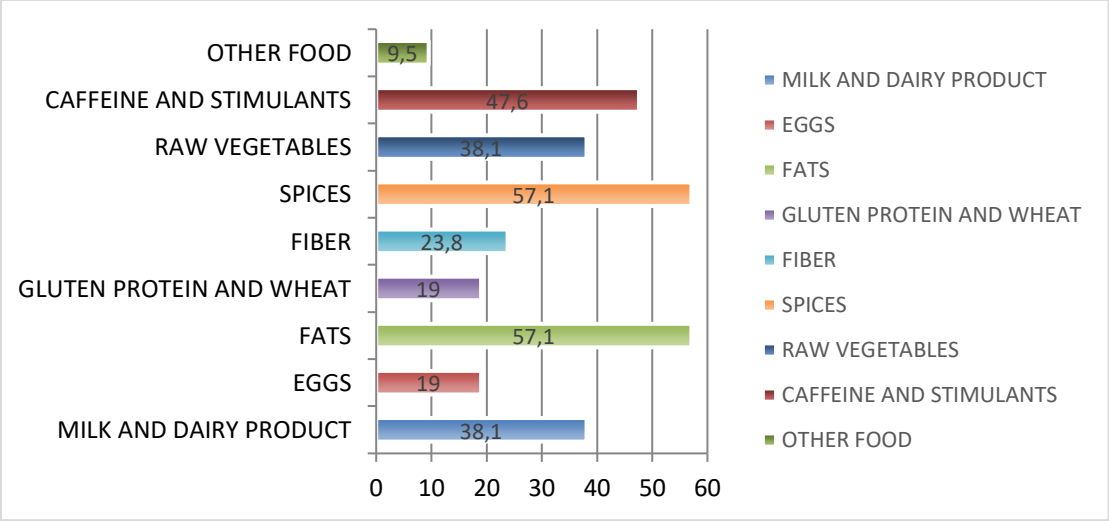


Fig. 18: Foods that cause harm

III. Methods of Treatment

III.1. Treatment with medications

III.1.1. Medicines used by patients

Based on our study population, the usage of medications for treating Crohn's disease was as follows (Fig.19):

- **Methotrexate and Azathioprine**: Most commonly used by 36.4% of patients.
- **Prednisolone**: Used by 31.8% of patients.
- **Infliximab**: Administered to 22.7% of patients.
- **Adalimumab**: Given to 4.5% of patients.
- **Other treatments**: Received by 31.8% of patients.

These figures illustrate the variety of medications used in managing Crohn's disease among the study participants, highlighting different therapeutic approaches and preferences in treatment.

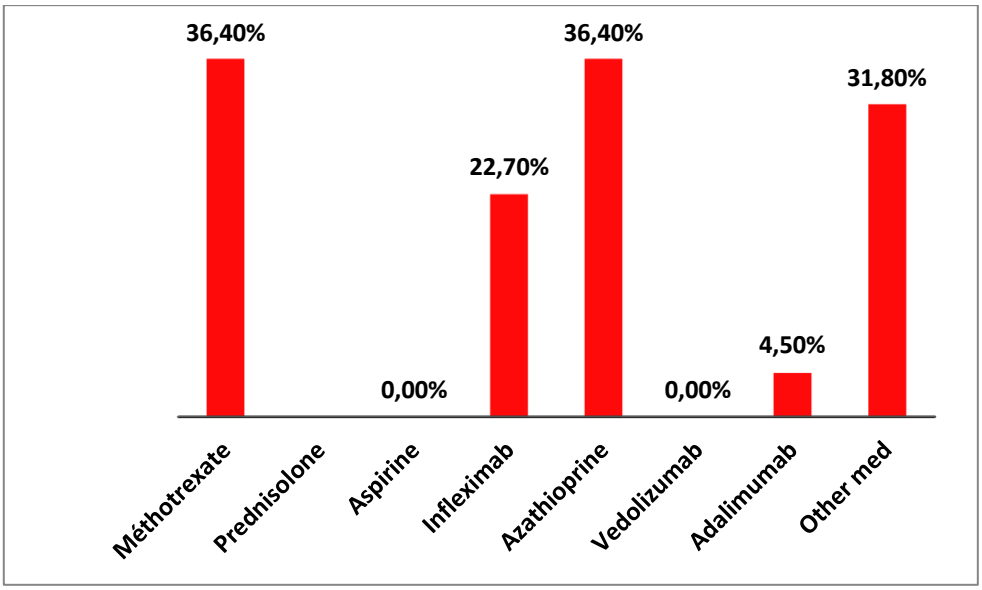


Fig. 19: Medicines used by patients

III.1.2. Benefit from medications

The results indicate that among the studied population (Fig.20):

- **No improvement**: 22.7% of patients did not experience any improvement in their condition.
- **Improvement**: The vast majority, 77.3% of patients, experienced improvement in their condition.

These findings suggest that while a significant majority of patients saw positive outcomes with their treatments, a notable proportion did not show improvement. This underscores the variability

in treatment responses among individuals with Crohn's disease and highlights the ongoing need for personalized approaches in managing the condition.

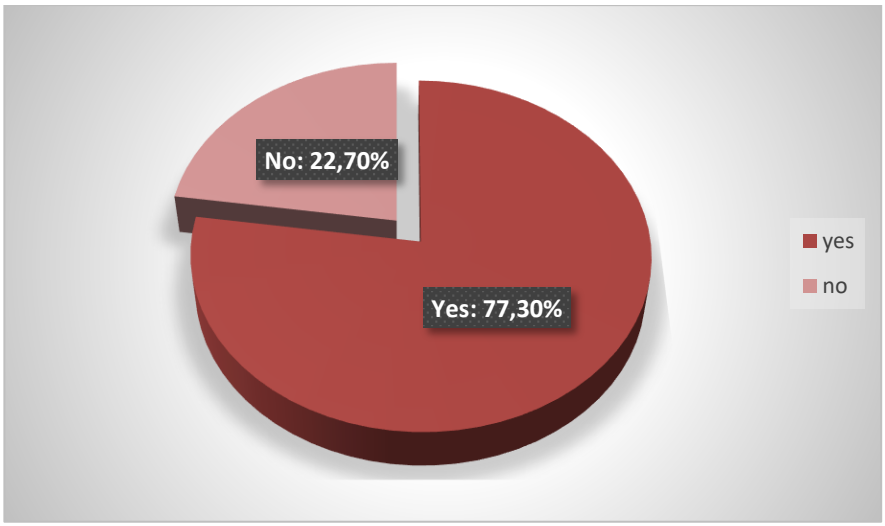


Fig.20: Benefit from medications

III.1.3. Noticed side effects when taking these medications

In our study population (Fig.21):

- **No side effects**: 55% of patients did not experience any side effects from their treatments.
- **Side effects**: 45% of patients reported experiencing side effects.

These results indicate that a substantial proportion of patients encountered side effects while undergoing treatment for Crohn's disease. Managing and minimizing these side effects are crucial aspects of patient care to ensure treatment adherence and overall well-being.

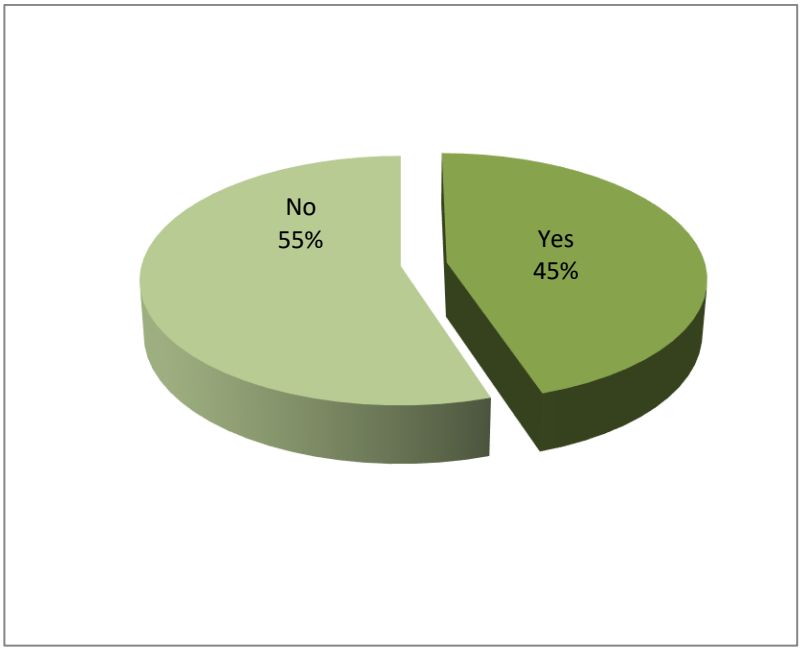


Fig. 21: Noticed side effects when taking these medications

III.1.4. Noticeable side effects

In our study population, the reported side effects among patients were as follows (Fig.22):

- **Nausea**: Experienced by the majority, 55.6% of patients.
- **Headaches**: Reported by 33.3% of patients.
- **Monitoring for osteoporosis**: Necessary for 22.2% of patients.
- **Abdominal pain**: Noted by 11.1% of patients.

These findings highlight the prevalence of specific side effects experienced by individuals undergoing treatment for Crohn's disease in our study. Managing these side effects is essential in optimizing patient comfort and treatment adherence.

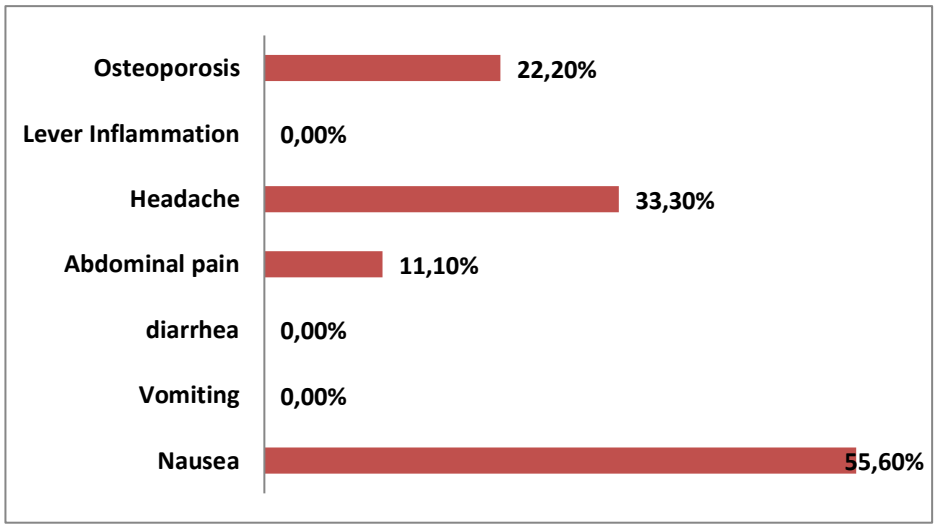


Fig. 22: Noticeable side effects

III.2. Herbal treatment

To manage symptoms and enhance quality of life for individuals with Crohn's disease, herbal treatments have been employed across different cultures for centuries to address digestive and inflammatory conditions. These natural remedies offer an alternative approach that aims to mitigate inflammation, foster healing, and promote overall gastrointestinal health.

Herbal treatments often include plants and botanical extracts known for their anti-inflammatory properties, such as turmeric, ginger, and Boswellia (Table III). These herbs may help alleviate symptoms like abdominal pain and discomfort associated with Crohn's disease. Additionally, herbs rich in antioxidants, such as green tea and chamomile, can support gut health by reducing oxidative stress and promoting tissue repair.

It's important to note that while herbal treatments can be beneficial, their efficacy and safety vary. Consulting with a healthcare provider knowledgeable about herbal medicine is crucial to ensure

proper use, minimize potential interactions with prescribed medications, and tailor treatments to individual needs.

In summary, herbal treatments represent a natural approach that may complement conventional therapies in managing Crohn's disease symptoms. Their potential to reduce inflammation and support gastrointestinal health underscores their role as part of a holistic approach to treatment.

Table III: Herbs use for treatment

WHAT HERBS DID YOU USE FOR TREATMENT?	AGREE %	STRONGLYAGREE %	DISAGREE %	NO OPINION %
TURMERIC	52.4	32.8	4.8	19
ALOE VERA	14.3	0	19	66.7
GINGER	38.1	0	33.3	28.6
SIBERIAN GINSENG	14.3	0	14.3	71.4
CHAMOMILE	30	0	20	50
OAKBARK	33.3	23.8	4.8	38.1
TEUCRIUMPOLIUM	28.6	23.8	4.8	42.9
FRANKINCENSE	30	20	10	40
POMEGRANATE	45.5	18.2	9.1	27.3
NECESSITYPAPER	35	10	5	50
ALOYSIACITRIODORA	59.1	9.1	4.5	27.3
OTHER HERBS	4 Answers - Anise - Cumin is excellent for pain - Carob plant - Fennel, anise, and coriander			

The predominant use of medicinal herbs such as turmeric, ginger, pomegranate, and Aloysia citriodora (lemon verbena) in our survey reflects their popularity among patients for managing symptoms of Crohn's disease. These herbs are valued for their rich content of active ingredients known for their anti-inflammatory properties and other beneficial components.

- **Turmeric** contains curcumin, which is well-known for its potent anti-inflammatory effects. It may help reduce inflammation in the gut and alleviate symptoms such as abdominal pain and diarrhea.
- **Ginger** is traditionally used to soothe digestive issues, including nausea and stomach discomfort. Its anti-inflammatory properties can also support overall gut health.
- **Pomegranate** is rich in antioxidants and polyphenols, which contribute to its anti-inflammatory properties. It may help reduce oxidative stress and support gastrointestinal healing.

- **Aloysia citriodora (Lemon Verbena)** is known for its digestive benefits and calming effects on the digestive tract. It can help alleviate digestive discomfort and promote overall gut health.

The popularity of these herbs among patients with Crohn's disease underscores their perceived effectiveness in managing symptoms like severe diarrhea and complications associated with inflammation. However, while these herbs offer promising benefits, it's essential for patients to discuss their use with healthcare providers to ensure they complement and do not interfere with prescribed treatments. Integrating these herbs into a comprehensive treatment plan under professional guidance can potentially enhance symptom management and improve quality of life for individuals with Crohn's disease.

III.2.1. Benefit from herbs

Based on our finding (Fig.23):

- **Improvement with herbs**: 81% of patients reported noticing a positive impact on their condition.
- **No improvement with herbs**: 19% of patients did not experience any noticeable benefit from using herbs.

These results indicate that a significant majority of patients perceived improvement in their symptoms when using herbs as part of their treatment for Crohn's disease. However, it's essential to consider individual variability in response to herbal treatments, and further research is warranted to better understand the efficacy and specific benefits of herbs in managing Crohn's disease symptoms.

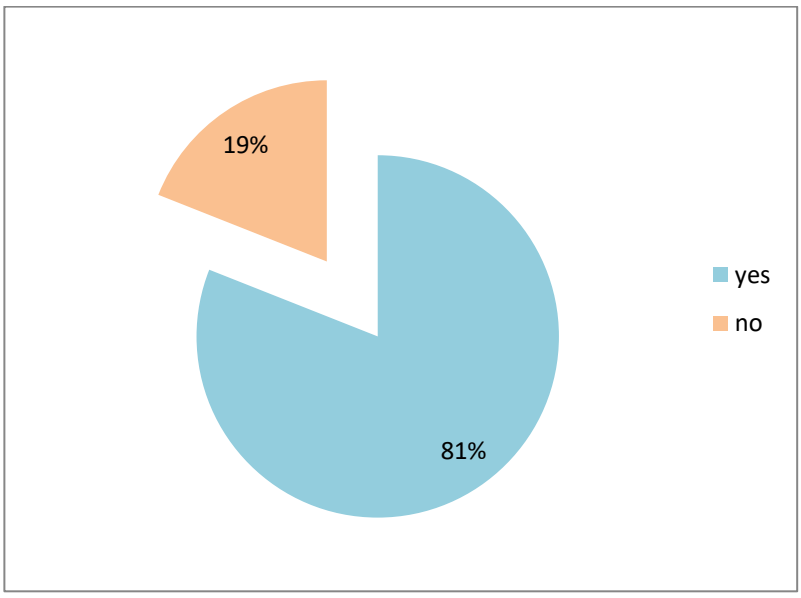


Fig.23: Benefit from herbs

III.2.2. Herb that helped the most

Among the responses indicating improvement with specific herbs:

- **Turmeric, Fennel, Anise**: This combination was mentioned as helpful by one respondent.
- **Fennel**: Another respondent highlighted fennel as beneficial.

These herbs, including turmeric, fennel, anise, and combinations like pomegranate with carob and juniper, reflect individual preferences and perceived effectiveness in managing symptoms associated with Crohn's disease. Each herb may offer unique properties that contribute to symptom relief, such as anti-inflammatory effects, digestive support, or antioxidant benefits. Integrating these herbs under professional guidance can help tailor treatment approaches to better meet individual needs and improve overall quality of life.

III.2.3. Noticed side effects when consuming herbs

Based on the results obtained from our study population (Fig.24):

- **Side effects noticed**: 16% of patients reported experiencing side effects when consuming herbs.
- **No side effects**: The vast majority, 84% of patients, did not notice any side effects from consuming herbs.

These findings suggest that the majority of patients perceive herbs as generally well-tolerated, with a relatively low incidence of side effects. However, it's important to acknowledge individual variability in responses to herbal treatments, and monitoring for potential interactions or adverse effects remains essential. Healthcare professionals should be consulted to ensure safe and effective use of herbs alongside conventional treatments for Crohn's disease.

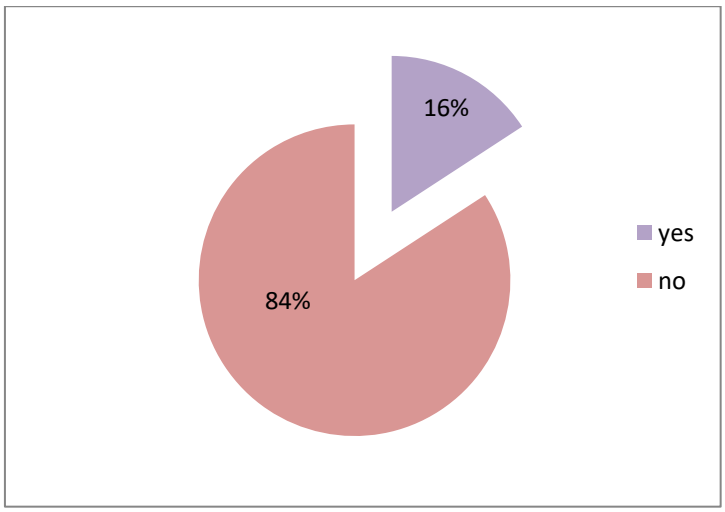


Fig.25: Noticed side effects when consuming herbs

III.2.4. Preferred type of medication

Regarding treatments in our study population (Fig.25):

- **Herbal treatment**: 48% of patients opted for herbal treatments.
- **Medications**: 43% of patients were treated with medications.
- **Other methods**: 9% of patients utilized another method for treatment.

These results highlight the diverse approaches taken by patients in managing Crohn's disease, with a significant proportion opting for herbal treatments alongside conventional medications or other methods. Individual preferences, perceived effectiveness, and considerations of safety and side effects likely influence these treatment choices.

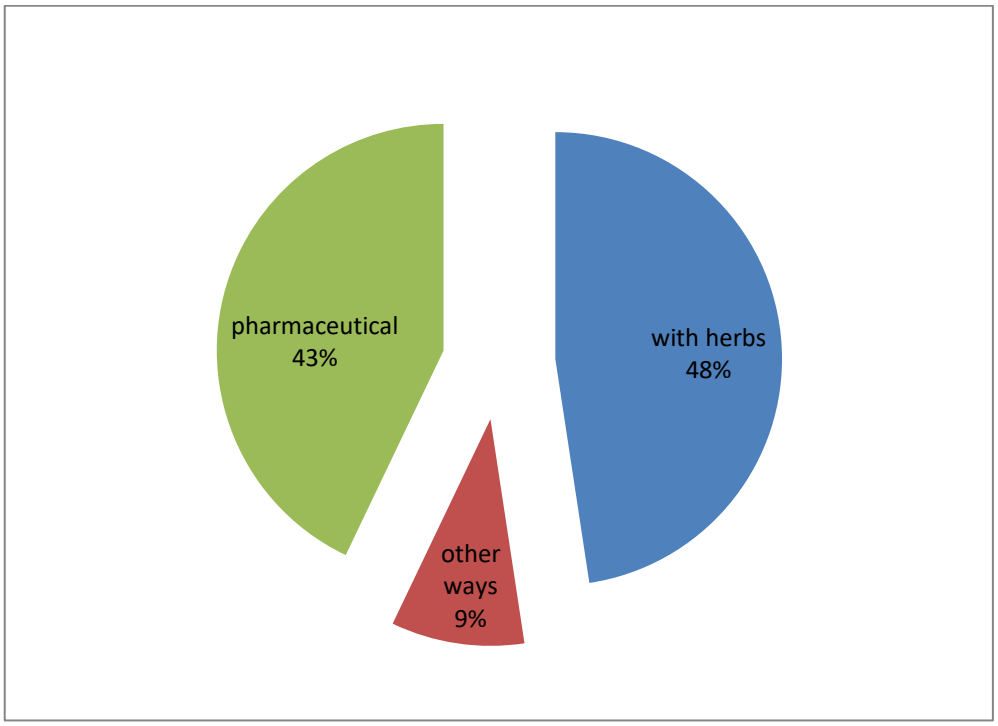


Fig.25: Preferred type of medication

Conclusion

Crohn's disease is a chronic inflammatory condition that primarily affects the gastrointestinal tract, characterized by unpredictable periods of flare-ups and remission. It falls under the category of inflammatory bowel diseases. Symptoms can vary widely. The exact cause of Crohn's disease remains complex and multifactorial, involving genetic predisposition, immune system dysfunction, and environmental factors. Management typically involves a combination of medications to control inflammation, alleviate symptoms, and maintain remission, alongside dietary modifications and in some cases, surgical interventions.

In the pursuit of alternative and complementary treatments, natural compounds such as curcumin and verbena are garnering attention for their therapeutic properties in managing Crohn's disease. Curcumin, derived from the rhizome of turmeric (*Curcuma longa*), is celebrated for its robust anti-inflammatory and antioxidant effects. It operates by inhibiting pivotal molecular pathways implicated in inflammation, including nuclear factor kappa B (NF-κB) and pro-inflammatory cytokines. Early clinical studies suggest that curcumin may play a role in inducing and maintaining remission in Crohn's disease by alleviating intestinal inflammation and improving clinical symptoms.

Verbena (*Verbena officinalis*), a medicinal plant with a rich historical background, possesses anti-inflammatory, antispasmodic, and immunomodulatory properties. Its active compounds, such as flavonoids and iridoids, are recognized for their ability to modulate immune responses and reduce intestinal inflammation. Preliminary research indicates that verbena may complement conventional therapies by mitigating gastrointestinal symptoms and enhancing overall well-being in patients with Crohn's disease.

This thesis thoroughly explores the mechanisms of action of curcumin and verbena through comprehensive analysis of clinical and preclinical data. It examines their potential as adjunctive treatments for Crohn's disease, highlighting both the benefits and limitations of these natural approaches. While promising, rigorous clinical studies are crucial to validate their efficacy, establish standardized treatment protocols, and evaluate potential interactions with existing therapies.

In conclusion, curcumin and verbena represent promising avenues in the management of Crohn's disease, offering a holistic and potentially synergistic approach alongside conventional treatments. Their integration into therapeutic regimens has the potential to improve clinical outcomes and enhance the quality of life for patients, signaling new possibilities in the treatment of inflammatory bowel diseases.

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ملخص

مرض كرون هو حالة التهابية مزمنة تؤثر غالبًا على الجزء العلوي من الأمعاء الدقيقة والأمعاء الغليظة، وتتميز بفترات من التصاعد والتلاشي للأعراض، يعد الكركم مادة مهمة. يتم استخدام الكركم بشكل رئيسي لاستخراج الكركمين، وهو مركب طبيعي نشط يأتي من جذر الكركم. الكركمين معروف بفعاليته البارزة كمضاد للالتهابات ومضاد للأكسدة، وأظهرت الأبحاث أنه يمكن أن يكون له تأثيرات إيجابية على الصحة، مثل تقليل التورم، تخفيف الألم، ودعم الصحة العامة للجهاز المناعي والهضمي. بالإضافة إلى ذلك، اللويزة هي نبات عشبي يُستخدم في الطب العشبي لتهدئة الأعصاب، وتقليل القلق، وتحسين عملية الهضم، وتخفيف الاضطرابات المعوية البسيطة، كما أن لها خصائص مضادة للالتهاب. وفقا لدراسة إحصائية موجهة لمرضى كرون أظهرت أن اغلبية المرضى حوالي 52.4% يستعملون الكركم في تخفيف الالتهاب وحدة المرض، كما ان 59.1% يستعملون اللويزة في تخفيف الألم والمضاعفات المعوية وبالتالي في ولاية سطيف الكركم واللويزة تعتبر خيارات مفيدة ومحتملة كجزء من نهج شامل لإدارة وعلاج مرض كرون.

الكلمات المفتاحية: مرض كرون، الجهازالهضمي، الكركم، االلويزة.

Abstract

Crohn's disease is a chronic inflammatory condition that often affects the upper part of the small intestine and the colon, characterized by periods of flare-ups and remission of symptoms. *Curcuma Longa* is considered a significant substance in this regard. It is primarily used to extract curcumin, a natural active compound derived from the turmeric root. Curcumin is well-known for its prominent anti-inflammatory and antioxidant properties, with research indicating potential positive effects on health such as reducing swelling, alleviating pain, and supporting overall immune and digestive health. Additionally, *Verbena Officinalis* is an herbal plant used in herbal medicine to calm nerves, reduce anxiety, improve digestion, and alleviate minor gastrointestinal disorders, also possessing anti-inflammatory properties. According to a statistical study focused on Crohn's disease patients, it was shown that the majority of patients about 52.4% use turmeric to alleviate inflammation and disease severity, as well as 59.1% *Verbena* to alleviate pain and intestinal complications. Therefore, in Setif, *Curcuma Longa* and *Verbena Officinalis* are considered useful and potential options as part of a comprehensive approach to managing and treating Crohn's disease.

Keywords: Crohn's disease, Digestive System, *Curcuma Longa* and *Verbena Officinalis.*

Résumé

La maladie de Crohn est une affection inflammatoire chronique qui affecte souvent la partie supérieure de l'intestin grêle et le côlon, caractérisée par des périodes de poussées et de rémission des symptômes. Le *curcuma Longa* est une substance importante dans ce contexte. Il est principalement utilisé pour extraire la curcumine, un composé actif naturel dérivé de la racine de curcuma. La curcumine est bien connue pour ses propriétés anti-inflammatoires et antioxydantes marquées, avec des recherches indiquant des effets positifs potentiels sur la santé tels que la réduction de l'enflure, le soulagement de la douleur et le soutien de la santé globale du système immunitaire et digestif. De plus, *Verbena Officinalis* est une plante herbacée utilisée en médecine traditionnelle pour apaiser les nerfs, réduire l'anxiété, améliorer la digestion et soulager les troubles gastro-intestinaux mineurs, tout en possédant également des propriétés anti-inflammatoires. Selon une étude statistique axée sur les patients atteints de la maladie de Crohn, il a été démontré que la majorité des patients environ 52.4% utilisent le curcuma pour soulager l'inflammation et la sévérité de la maladie, ainsi que 59.1% *Verbena Officinalis* pour soulager la douleur et les complications intestinales. Ainsi, à Sétif, le curcuma et *Verbena Officinalis* sont considérés comme des options utiles et potentielles dans le cadre d'une approche globale pour la gestion et le traitement de la maladie de Crohn.

Mots clé : Maladie de Crohn, système digestif, *Curcuma Longa* et *Verbena Officinalis.*