

## ROLE OF AYURVEDIC HERBS IN THE MANAGEMENT OF CELIAC DISEASE

### Abstract

~~An autoimmune disorder affecting the small intestine is known as celiac disease or gluten-sensitive enteropathy.~~ Celiac disease or gluten-sensitive enteropathy is an autoimmune hypersensitivity disorder affecting the small intestine. It occurs due to an ~~inappropriate~~ immune reaction to gluten, which results in inflammation and damage to the small intestine. One of the most prevalent illnesses, celiac disease, is brought on by both environmental (gluten) and genetic causes of human leukocyte antigen (~~HLA~~HLA) and non-HLA genes~~}. The prevalence of celiac disease has been estimated to approximate 0.5%-1% in different parts of the world. Due to improved physician awareness and expertise, as well as the widespread use of extremely sensitive and precise diagnostic tests for celiac disease, the prevalence of celiac disease has considerably grown in the past 30 years. While older children have either limited or unusual symptoms, only a small percentage of celiac patients have the classic signs of the condition like chronic or intermittent diarrhea, failure to thrive, weight loss, delayed puberty, short stature, nausea, vomiting, chronic abdominal pain, abdominal distension, chronic constipation. Early detection of celiac disease is crucial to preventing long-term consequences. The only cure is a lifetime gluten-free diet. In Ayurveda, it can be correlated with Grahani Dasha. Grahani is described as an Agni Adhithana by most of Acharya. Mandagini is the root cause of Ama Dasha, and it is a crucial factor for ~~manifestation of the~~ manifestation of most diseases. The treatment approach of celiac disease in Ayurveda medicinal science involves the intake ~~the of~~ various preparations of some specific medicinal plants like Kutaja (*Holarrhena antidysenterica*) Pippali, (*Piper longum* Linn.), Chitraka, (*Plumbago zeylanica*) Guduchi, (*Tinospora cordifolia*) Ashwagandha, (*Withania somnifera*), Haridra (*Curcuma longa* Linn.), etc which have Agni Deepana and Ama Pachana properties. These illness-specific medicinal herbs help ~~in the normalization of digestive fire and evicting~~ normalize digestive fire and evict "Ama" toxins from the body channels, which ~~pacified~~ pacify the vitiated Agni and maintain homeostasis among vitiated Doshas.~~

**Keywords:-** Ayurvedic Herbs, Ashwagandha, Celiac disease, Chitraka, Grahani, Grahani Dasha, Grani Roga, Guduchi, Haridra and Kutaja.

### INTRODUCTION

Celiac disease (CD) is an immune-mediated systemic disease triggered by the intake of gluten and related Prolamins in genetically susceptible individuals, characterized by the presence of various combinations of small intestinal damages, ~~celiac-celiac~~ celiac-specific antibodies, human leukocyte antigen (HLA)HLA-DQ2 or HLA-DQ8, and gluten-dependent clinical manifestations<sup>1</sup>. Gluten is found in wheat, barley, rye, and oats<sup>2</sup>. CD-specific antibodies comprise autoantibodies against ~~type 2 TG2~~ transglutaminase (TG2), ~~including~~ endomysial antibodies (EMAsEMAs), and antibodies against deamidated ~~forms of~~ gliadin peptides. Celiac disease is a common disorder with about 1% prevalence of biopsy-proven disease. In East Asia and Central Africa, it is assumed to be uncommon. Although autoantibodies, turning celiac disease into a systemic disease develops in genetically susceptible individuals, environmental factors might affect the risk of developing celiac disease or the timing of its presentation. Even after gluten is added, there is no proof that breast milk increases the risk of celiac disease. The

cumulative prevalence of both autoimmunity (positive serology) and celiac disease in later childhood is unaffected by the earlier intake of gluten. It is recommended to introduce gluten into a baby's diet any time between 4 and 12 months of age. Due to the association between repeated rotavirus infections and a higher risk of celiac disease, it has been hypothesized that infectious agents are responsible for the condition.<sup>3</sup> It is plausible that contact with gliadin ~~at a time~~—when there is ongoing intestinal inflammation alters intestinal permeability, and the enhanced antigen presentation can increase the risk of developing celiac disease, at least in a subset of persons. The likelihood of getting celiac disease has been linked to the manner of delivery, socioeconomic level, season of birth, and medication usage—, however, the data is conflicting. When a person with celiac disease consumes gluten, their immune system's white blood cells assault and damage the intestinal villi—~~T~~. This ongoing assault damages the tiny intestinal villi permanently over time by altering their structure. Since intestinal villi are involved in both the absorption of nutrients from food and the defense against dangerous microorganisms, celiac disease affects both the immune system and digestion. The exact mechanism of how celiac disease occurs is not fully understood. However, a mix of genetic and environmental variables is likely ~~to be~~ responsible for its development. In those who are genetically susceptible to the disorder, some experts think that ~~celiac disease is brought on by an infection or another environmental event~~ an infection or another environmental event brings on celiac disease. ~~such~~ Such patients are then unable to absorb the food nutrients in good aspect, which leads to many physiological disturbances, ~~and~~ few of those being loss in bone density, neurological diseases, etc.<sup>4</sup>

The small intestine's enterocytes are damaged, ~~which results in the symptoms of celiac disease~~ resulting in celiac disease symptoms. In the full-blown clinical picture, the typical features of the small intestine are chronic inflammation and villi atrophy.<sup>5</sup> An individual has to have HLA-dominant DQ2 or DQ8 genes.

An essential protein ~~involved~~ in the illness process is an antibody to tissue transglutaminase. The disease is caused by the immune system responding negatively to gluten. Other possible paths that lead to the illness have been suggested, ~~though~~ however. Through its up-regulation of IL-15 production, the glycoprotein gliadin, ~~which is found in gluten~~, found in gluten directly damages enterocytes.

According to ~~certain particular~~ research, early childhood gastrointestinal infections may have a connection to the eventual onset of celiac disease. ~~This makes sense given the organ in question~~ This makes sense, given the organ in question, but ~~it's—it is~~ also probably directly related to the theory that ~~celiac disease~~ CD is an immune system malfunction. The diagnosis of celiac disease is frequently made using IgA antibodies against tissue transglutaminase and smooth muscle endomysium. However, ~~only~~ about 5% of patients with ~~celiac disease~~ CD have a deficiency of this immunoglobulin.<sup>6</sup> Clinical features of Celiac disease vary considerably. The intestinal type of CD is ~~characterised~~ characterized by diarrhoea, appetite loss, abdominal distention, and failure to thrive. It is more frequently found in the pediatric population and children under ~~the age of~~ three. Diarrhoea, bloating, constipation, stomach discomfort, and weight loss are common complaints among older adults and children. However, the malabsorption syndrome accompanied ~~with~~ by severe asthenia, weight loss, and persistent diarrhoea is ~~extremely~~ exceptionally uncommon in adulthood. This phenotype, albeit seldom seen, can lead to hospitalization because of substantial hypoalbuminemia, sarcopenia, cachexia, and electrolyte abnormalities. On the other hand, it is more common to appear with symptoms similar to those of dyspepsia or irritable bowel syndrome (~~IBS~~ IBS), such as constipation or alternating bowel movements, nausea, and occasionally vomiting.<sup>7</sup> All individuals with celiac disease are advised to adhere to a rigorous gluten-free diet. ~~It is advisable to follow this adherence plan while being~~ Following this adherence plan is advisable while closely supervised by experts, such as ~~a dietitian~~ dietitians. On a gluten-free diet,

symptoms often ~~get better~~ improve after a few days or weeks. Unresponsive patients require a reconsideration of the diagnosis and an evaluation of their diet compliance. Serology testing can assess compliance. Non-compliance can be unintentional in an individual ~~who may be~~ still ingesting gluten without realizing it.<sup>8,9</sup> Other tests include looking at the impact of malabsorption (due to ~~celiac disease~~ CD). The whole blood count, iron reserves, folate, ferritin, vitamin D, ~~and other~~ fat-soluble vitamin levels, and bone mineral density may all be tracked. It is debatable how to treat patients whose duodenal biopsies reveal nothing wrong but whose serology is positive. The diagnosis is often not definitive in many cases. Despite a tiny gut biopsy finding no abnormalities, some people have pertinent symptoms. There is also seronegative celiac disease. This term describes the reverse situation when, despite typical symptoms, there is no serological evidence of the disease, ~~and but~~ there is significant villous atrophy of duodenal biopsy. Currently, the only recommended treatment for celiac disease is a gluten-free diet. Maintaining this may ~~be difficult not be easy~~ and has a ~~big significant~~ effect on the lives of those who are impacted. Research into potential non-dietary treatments that might help gluten intolerance in individuals with celiac disease is ongoing. Immune modulators are a primary topic of interest for this field of research.<sup>10</sup> Other approaches, like immunizations or ingesting substances that would change the toxicity of gluten, are also being explored. None, ~~though~~, have advanced to the point where they may be suggested or authorized for this ~~kind of~~ therapy. Few people with celiac disease benefit from corticosteroids.

#### AIMS AND OBJECTIVES:-

1. To reveal hidden facts in Ayurveda for celiac disease.
2. To collect the research on ayurvedic treatment for celiac Disease

#### MATERIAL AND METHODS: -

The study's primary materials were collected from *Ayurvedic* classics like the *Charaka Samhita* and *Sushruta Samhita* ~~as well as contemporary textbooks using digital media, and contemporary textbooks using digital media, such as~~ the *AYUSH A.Y.U.S.H.* Research Portal, Pubmed, Google ~~scholar~~ Scholar, and other subject-related websites on the internet.

#### AYURVEDIC PERSPECTIVE OF CELIAC DISEASE

Although the exact correlate of celiac disease is not available in *Ayurvedic* classics, based on similarities of symptoms, this disease may be assumed ~~equivalent to a disease named Grahani Dosha to be equivalent to Grahani Dosha, which has been~~ explained in *Ayurveda* in detail. As per the *Ayurvedic* texts, *Grahani Dosha* comes into existence with *Agni-Dusti* (the derangement of digestive fire).<sup>11</sup> Digestion is ruled by *Agni*, supported by the three *Dosha* (body humours). Hence ~~any derangement in Agni or any imbalance of one or more Dosha is capable of hampering the process of, any derangement in Agni or imbalance of one or more Dosha can hamper~~ digestion, ultimately leading to ~~a the~~ disease of *Annavaha Srotas*. According to *Ayurvedic* literature, wheat is endowed with *Madhura Rasa* and *Sheet-Snigdha-Guru Guna*. It increases *Kapha Dosha* and brings about *Mandagni* (weakness of digestive fire) ~~which ultimately leads to the formation of Ama (toxins), which is~~ responsible for the existence of *Grahani Dosha*.<sup>(12,13)</sup> Following the medical discipline of *Ayurveda*, celiac disease is a form of ailment ~~that is~~ largely brought on by a weaker digestive fire in the digestive system, known as *Agni* or *Jathragni*. Food digestion is hampered by lesser digestive fire, and when food is not digested, it either moves upwards or downwards. It can induce small intestine mucosal inflammation, villous atrophy, and spells of constipation when it goes downhill. The food is not broken down into "*Sam*" parts during this

Formatted: Font: Italic

cycle of indigestion; ~~rather instead~~, it is broken down into "Ama" parts. In addition, because of all these digestive troubles, the bone tissues are not ~~properly adequately~~ fed, which causes osteoporosis. Other *Dhatus* like *Rasa*, *Asthi Kashya*, and *Majja Kashya* are also ~~then not adequately nourished~~ ~~not adequately nourished~~, leading to diseases associated with them. ~~Function all weak Agni i.e. Ama Dosha is the result of~~ ~~All weak Agni, i.e., Ama Dosha, result from~~ faulty food digestion caused by *Mandagni*. The majority of ailments have this *Ama Dosha* as their underlying cause. It is crucial to understand the pathophysiology of *Grahani Roga*. *Grahani* is ~~difficult-challenging~~ to diagnose and ~~tough-tricky~~ to cure because it is one of the eight main disorders. According to *Ayurveda*, the symptoms include *Muhu Baddha* and *Drava Mala Pravritti* (either constipation or loose faeces), *Apachana* (indigestion), *Aruchi* (anorexia), and *Udara Shoola* (abdominal discomfort).<sup>14</sup> Treatment of *Grahani* ~~dosha-Dosha~~ in *Ayurveda*, like other diseases, proceeds with ~~the adoption of adopting~~ *Sanshodhan-Vidhi* (emesis), ~~and it is complemented by use of palliative medicines~~ ~~complementing palliative medicines~~.<sup>15</sup> The use of medicinal herbs with *Agni Deepana* and *Aam Pachana* characteristics is part of the *Ayurvedic* medical science's approach to treating celiac disease. These therapeutic plants for certain illnesses aid in restoring a regular digestive fire and expelling "Ama" poisons from the body's channels. Thus, this line of natural treatment approaches through the intake of medicinal plants helps ~~in the complete reversal of~~ ~~completely reverse~~ the condition and enables holistic health benefits.<sup>16</sup>

When the food ingests, it is left undigested; ~~it's it is~~ then transformed into "Ama" (toxins), and it ~~then~~ either travels upwards or downwards before causing any disease. The direction and the seat where this *Ama* gets lodged becomes the ~~root origin of the disease~~ ~~disease's root origin~~, and the signs/symptoms are then concentrated around that specific tissue/organ. So, treating signs ~~are never a priority in Ayurveda and it's only when starts~~ ~~never a priority in Ayurveda and only when~~ addressing the root cause. Thus, *Ayurveda* can alleviate all the signs and address ailments. In particular, if the "Ama" or toxins move downward, it causes inflammation of the small intestine mucosa and constipation ~~as well~~ by unbalancing the bowel movements.<sup>17</sup>

## HERBS EFFECTIVE IN CELIAC DISEASE –

The immune system's response to gluten in the small intestine results in the autoimmune illness known as celiac disease. Some *Ayurvedic* herbs such as *Kutaja*, *Pippali*, *Chitraka*, *Guduchi*, *Ashwagandha*, and *Haridra* ~~were found effective in the treatment of~~ ~~effectively treat~~ celiac disease. A detailed description of these herbs is given below-

**1. Kutaj:- *Holarrhena antidysenterica* (syn. *H. pubescens*)** *Rasa* of *Kutaja* is *Tikta*, *Kashaya*, *Laghu*, *Rooksha Guna*, *Sheeta* and *Katu Vipaka* & *Veerya*.<sup>18</sup> Chemical ~~constituents~~ ~~constituents~~ steroidal alkaloids, such as conanines, 3-aminoconanines, 20-aminoconanines, 3-aminopregnans, 3,20-diaminopregnanes and their derivatives. A new steroidal alkaloid was isolated and characterized; ~~designated as and designated~~ holadysenterine. Corresponded to the molecular formula  $C_{23}H_{38}N_2O_3$ .<sup>19</sup> The stem bark of *Holarrhena antidysenterica* also contains conessine ( $C_{24}H_{40}N_2$ ), isoconessine ( $C_{24}H_{40}N_2$ ), conessimine/ isoconessimine ( $C_{23}H_{38}N_2$ ), conarrhimine ( $C_{21}H_{34}N_2$ ).<sup>20</sup> Methanolic leaf extract of *Holarrhena antidysenterica* revealed inhibition of rat paw edema induced by carrageenan. Furthermore, the Methanolic extract of *Holarrhena antidysenterica* suppressed acetic acid-induced writhing response ~~in dose dose dependent manner~~ ~~dose-dependently~~ and demonstrated the analgesic effect by improving ~~tail-tail~~ flick latency.<sup>21</sup> Ethanolic extract of *H. antidysenterica* exhibited an analgesic effect by suppressing writhing response in albino mice. In 2,4-Dinitrobenzene

sulfonic acid-induced colitis in male albino ~~wistar~~ Wistar rats, methanolic bark extract of *H. antidysenterica* demonstrated increased levels of glutathione and superoxide dismutase and lowered levels of nitric oxide and malondialdehyde. The lower nitric oxide level suggests ~~that~~ the anti-inflammatory impact may be due to ~~a decrease in~~ decreased iNOS production. Treatment with *H. antidysenterica* also inhibited goblet cell rupture, inflammatory cellular infiltration, and mucosal layer inflammation.<sup>22</sup> Rats' dry weight of excrement increased significantly when exposed to ethanolic seed extracts of *H. anti-dysenterica*, ~~whereas. In contrast,~~ their defecation ~~decreases~~ decreased in castor oil, and *E. coli*-induced diarrhea decreased.<sup>23</sup> Rats with castor oil-induced diarrhea had significantly less watery diarrhoea and motility in the small intestine when given the *H. antidysenterica*-marketed product *Kutaja Parpati Vita*. Additionally, it demonstrated a note-worthy 67.55% defense against ~~diarrhea~~ enteropooling caused by castor oil<sup>24</sup>. A well-known plant called *Kutaja* controls the elevation of the *Pitta* and *Kapha Doshas*. It is a fantastic plant ~~that is~~ used to cure irritable bowel syndrome, diarrhea, and other conditions. Bark, seeds, flowers, and fruits are all excellent sources of Medicine.

Formatted: Font: Italic

Formatted: Font: Italic

**2. Pippali (*Piper longum* Linn.):**- *Pippali* belongs to the *piperaceae* family. *Ayurvedic* properties of *Pippali* ~~is are~~ *Katu, Tikta, and Madhura Rasa, Laghu, Snigdha Guna, and Madhur Vipaka*<sup>25</sup>. It is one of the prime *Rasayana* (rejuvenator) drugs in *Ayurveda* and is widely used to treat various diseases, especially for ~~the treatment of~~ creating intestinal disorders.<sup>26</sup> ~~In~~ <sup>26</sup> *In Ayurveda*, this plant's root is ~~referred to as~~ called *Pippali Mula*, ~~while. At the same time,~~ its fruits (spike) are mostly utilized for *Rasayana*. Chemical Constituents Two alkaloids piperlongumine & piperlonguminine, n- hexadecane, n- heptadecane, n-octadecane, n-nonadecane n-eicosane, n-heneicosane, n-thujene, terpinolene, zingiberene, p-cymene, p-methoxy acetophenone, traces of dihydrocarveol, phenyl ethyl alcohol & two sesquiterpenes; piperine, piplartin, triacotane, dihydrostigmasterol, an unidentified steroid, reducing sugar, glycosides, sesamin & methyl- 3,4,5- tri methoxycinnamate (root); major alkaloid piperine & sesamin (stem& fruit); sesquiterpene hydrocarbon, caryophyllene, a sesquiterpene alcohol, carbonyl compound (essential oil), N-isobutyldeca- trans- 2-trans- 4- dienamide, piperine, piplartine & a lignan d-sesamin, two piperidine alkaloids piperonaline& piperundecalidine (fruit), sylvatinsesamin & diaeudesmin (seed).<sup>27</sup> A decoction of *P. Longum* fruits has been shown to have a significant anti-inflammatory effect in rats with edema caused by carrageenan.<sup>28</sup> Rat paw edema caused by carrageenan leukotrienes' Cox-1 inhibitory action and prostaglandin are inhibited by *P. longum* extract and piperine, which has anti-inflammatory properties.<sup>(29-30)</sup>

According to Stohr JR et al. (2001), ~~Piperine~~ piperine and extracts from piper have an inhibitory effect on leukotrienes' COX-1 inhibitory action and prostaglandin, which results in anti-inflammatory activity.<sup>31</sup> The antioxidant activity of *Amrita Bindu*, a mixture of herbs (*Plumbago zeylanica* and *Cyperus rotundus*), spices (*Piper nigrum*, *Piper longum*, and *Zingiber officinale*), and salts ~~was were~~ examined. Using the following order, the investigation showed the components' potential as antioxidants-; *Zingiber officinale, Plumbago zeylanca, Piper nigrum, Piper longum, Cyperus rotundus*, and Pluto.<sup>32</sup> *P. longum* root is used for opioid-type analgesia using the rat tail-flick method, while ibuprofen and pentazocine are used as pharmacological controls for NSAID-type analgesia using the acetic-acid writhing method. Mice and rats were ~~administered an aqueous suspension of P. longum root powder orally~~ orally administered an aqueous *P. longum* root powder suspension.- The study found that *P. longum* root had strong NSAID-type analgesic effects but minimal opioid action.<sup>33</sup> In addition to the water decoction of *P. longum* and the colloidal solution of *Ferula asafoetida*, Agrawal et al. (2000) [11] reported the antiulcer activity was demonstrated by water decoction of ginger, one

of the constituents of *Mahakasyaya* drugs, which has been reported to protect against [CRSC.R.S.-](#), [ASPA.S.P.-](#), and PL-induced gastric ulcers in rats. In a dose- and time-dependent manner, piperine, an alkaloid of *P. longum*, slowed the stomach emptying of solids/liquids in rats and gastrointestinal transit in mice. The inhibitory effect of piperine on stomach emptying occurs independently of the release of gastric acid and pepsin.<sup>34</sup>

**3. *Guduchi* (*Tinospora cordifolia* (Wild.)—*Guduchi*)** belongs to the *Menispermace* family. Rasa is *Tikta*, *Laghu*, *Snigdha* in *Guna*, *Ushna* in *Veerya*, and *Madhur* in *Vipaka*<sup>35</sup>. It [harmonises-harmonizes](#) the body's *Tridosha*. *Guduchi* is a good source of antioxidants. It also has antiviral, antipyretic, and wound-healing properties.<sup>36</sup> Many chemicals have been discovered ~~from in~~ *T. cordifolia*, including phenolic compounds, aliphatic compounds, steroids, glycosides, alkaloids, and diterpenoid lactones. A few of the *Ayurvedic* benefits of *T. cordifolia* are *Aruchinashaka*, *Dipana*, *Agnidipana*, *Chardihara*, *Trishnahara*, and *Trishnanashaka*.<sup>37</sup> It has been shown that the ulcer index total acidity falls when a *T. cordifolia*-containing formulation is used, the pH of the stomach fluid of rats ligated with pylorus rises, and rats' ethanol-induced gastric mucosal damage reduces.<sup>38</sup> In rats, the carrageenin-induced acute and chronic inflammation was significantly reduced by the aqueous extract of *Tinospora cordifolia*; this reduction was comparable to that of [NSAIDSN.S.A.I.D.S](#). The local reaction of living mammalian tissues to any kind of agent-induced harm is known as inflammation. It is [a protective response of the body/the body's protective response](#) to get rid of or stop the spread of an inflammatory substance. It is categorized as [either acute or chronic depending on the host's defense capability and the length of the response](#) acute or chronic depending on the host's defense capability and the response length. Acute inflammation is characterized by several key elements, including the build-up of fluid and plasma, intravascular platelet activity, and polymorphonuclear neutrophils acting as inflammatory cells.<sup>39</sup> In the early stages of inflammation, caused by carrageenan, histamine, 5-hydroxytryptamine, and bradykinin are the first mediators that may be detected; prostaglandins are detected in the later stages of inflammation. According to a study, *Guduchi* Ghana made using the traditional way significantly reduces [the amount of edema caused by carrageenan, suggesting that it prevents fluid exudation and consequently the amount of edema caused by carrageenan, suggesting that it prevents fluid exudation and, consequently,](#) acute inflammation. It could be explained by *Guduchi* Ghana's capacity to alter the function of different chemical mediators of inflammation, such as histamine and 5 [HTH.T.](#), during the early stages of inflammation by either attenuating the synthesis of these mediators or [by](#) activating them at the receptor level.<sup>40</sup> Thus, it has been demonstrated that *Guduchi* Ghana cooked traditionally has a notable anti-inflammatory effect. <sup>(39,40)</sup> [In rats used to test this activity, a reduction in ulcer index and a dose-dependent anti-diarrheal effect were observed](#) A reduction in ulcer index and a dose-dependent anti-diarrheal effect were observed in rats used to test this activity. Additionally, there was a decrease in stomach capacity and an increase in pH in the stomach.<sup>41</sup> PGE2, proangiogenic factors (VEGF, EGF), and anti-inflammatory cytokines (IL-4, IL-10) are increased by the epoxy clerodane diterpene that is isolated from this plant.<sup>42</sup> Its extract had protective effects in an 8-hour model of ulceration in mice generated by restraint stress, and the outcomes were similar to those of diazepam.<sup>43</sup>

**4. Ashwagandha (*Withania somnifera*):** - *Ashwagandha* (*W. somnifera*) belongs to the genus *Withania* and the family *Solanaceae*. Ras is *Katu*, *Tikta*, *Kashaya*, and *Guna* is *Snigdha*, *Laghu*, *Veerya* and *Vipaka* also *Guna*, *Snigdha*, *Laghu*, *Veerya* and *Vipaka*, and *Ushna* and *Katu*.<sup>44</sup> It balances *Tridoshas*, especially *Kapha* and *Vata*. *Ashwagandha* is an **important essential** source of many medicinally and pharmacologically **important-necessary** chemicals such as Alkaloids (isopelletierine, anaferine, cuseohygrine, anahygrine, etc.), steroidal lactones (withanolides, withaferins), and saponins are major chemical constituents.<sup>45</sup> Withaferin A and 3-b hydroxy 2-Dihydro withanolide F isolated from *ashwagandha* - *Ashwagandha* shows promising antitumoral, immunomodulating **as well as antibacterial-antibacterial** and anti-inflammatory properties. The bark powder is an appetizer, carminative, and antihelminthic and hence used in abdominal pain, constipation, and worms. It affects the heart, purifies the blood, and reduces *Ashwagandha*. *It* has been widely studied for its various **Pharmacological activities like pharmacological activities, such as** anti-oxidant, anxiolytic, adaptogen, memory enhancing, anti-inflammatory, and antitumor properties. Many diseases linked to inflammation in the body, including diabetes, cancer, neurological diseases, autoimmune diseases, respiratory diseases, and cardiovascular diseases, are being researched concerning *Ashwagandha*, or *Withania somnifera*. Preclinical research has shown that this plant inhibits inflammatory markers such as cytokines (like TNF- $\alpha$  and IL-6), nitric oxide, and reactive oxygen species, **which in turn reduces inflammation and regulates reducing inflammation and regulating** mitochondrial activity and apoptosis. Meanwhile, *Ashwagandha* root powder's possible inhibitory action in lupus-ridden mice was shown in cases of proteinuria and nephritis.<sup>46</sup> Evidence from a study by Kanjilal et al. suggested<sup>47</sup> that people with arthritis may benefit from applying *Ashwagandha* extract for eight to twelve weeks.<sup>47</sup> A study on the impact of *Withania somnifera* root powder on the stimulation of immunological activity in immunodeficient mice validated the immunomodulatory effect. When *Withania somnifera* is administered, it has been observed to raise the overall count of white blood cells and bone marrow cells, as well as the titer of circulating antibodies and antibody-producing cells. It also promotes the phagocytosis of macrophages and the synthesis of immune cells.<sup>48</sup>

*Ashwagandha* **also** has several additional benefits, including hypolipidemia, immunomodulation, and antibacterial cardiovascular protection. Moreover, *somnifera* has demonstrated its ability to regulate apoptosis, lessen reactive oxygen species, adjust mitochondrial activity, and lower inflammation.<sup>49</sup> **Moreover** <sup>49</sup> **Moreover**, it can improve endothelial function. Traditional medicine uses withaferin-A, an essential phytoconstituent of *W. somnifera* that belongs to the withanolides class, to treat a wide range of illnesses.<sup>50</sup> Although *Ashwagandha* helps promote better digestive health, **it's-it is** critical to comprehend the connection between gut health and general well-being. **Food digestion, nutrient absorption, waste removal, and the preservation of a balanced gut microbiota are all handled by the digestive system. The digestive system handles food digestion, nutrient absorption, waste removal, and the preservation of a balanced gut microbiota.** An unbalanced digestive system can result in bloating, constipation, diarrhea, and inflammation, among other symptoms and health problems. *Ashwagandha* may help regulate the production of stomach acid, which helps lessen symptoms of acid reflux and ulcers, as well as enhance digestion and nutritional absorption by encouraging the growth of beneficial gut flora.<sup>51</sup>

**5. Chitrak (*Plumbago zeylanica*):** - *Plumbago zeylanica* Linn. (*Chitraka*) is one of the most important plants. A member of the *Plumbaginaceae* family is *Plumbago zeylanica* Linn. *Rasa-Katu*, *Guna-Laghu*, *Tikshna*, *Ruksha*, *Virya-Ushna*, and *Vipaka-Katu* are some of the characteristics of *Chitraka*.<sup>52</sup> chemical components of *Chitraka* include flavonoids, alkaloids,

glycosides, steroids, triterpenoids, saponins, tannins, coumarins, phenolic compounds, naphthoquinones, carbohydrates, fixed oil and fats and proteins. Among them, the most ~~important-critical~~ chemical constituent is ~~Plumbagin which is chiefly present in the roots of Chitrak and the plant with plumbagin, which is chiefly present in the roots of Chitrak and the plant and has~~ incredible curative qualities. Sheeja et al. used in vivo experimental models to study the anti-inflammatory properties of acetone and petroleum ether extracts of *Plumbago zeylanica* L.<sup>53</sup> ~~leaves-<sup>53</sup>leaves~~ at two dose ~~levels~~ (200 and 400 mg/kg, p.o.). ~~Rats' inflammation caused by carrageenan was considerably reduced by the acetone extract~~ ~~The acetone extract considerably reduced the inflammation caused by carrageenan in rat~~ as compared to the control group. According to the study, the extract's anti-inflammatory properties may be due to a decrease in prostaglandin synthesis and release as opposed to inflammatory chemicals that have already been produced.<sup>54</sup> *Plumbago zeylanica* L. dichloromethane extract was tested at ~~doses~~ ~~of~~ 250 mg/kg and 500 mg/kg by Subra Maniyan et al. in response to carrageenan-induced paw edema. According to a study, edema's inhibitory impact was on par with ~~that of~~ the common medication diclofenac. According to the study, its ability to scavenge free radicals and defend against apoptosis may be responsible for the inhibitory effect.<sup>55</sup> The effects of aqueous extract of *Plumbago zeylanica* L. root on acute stomach ulceration in albino rats caused by aspirin and indomethacin. Together with negative and positive control groups, they calculated and compared the ~~ulcer score, ulcer index, and percentage protection of the extract~~ ~~extract's ulcer score, index, and percentage protection~~. At 25, 50, and 100 ml/kg, the extract showed significant dose-dependent suppression of aspirin-induced stomach mucosal damage; at 50 and 100 mg/kg, respectively, the extract demonstrated inhibition of indomethacin-induced ulcer.<sup>56</sup>

In the conventional medical system, *Plumbago zeylanica* L. has been highly recommended for its ability to heal wounds. Significant wound healing activity of *Plumbago zeylanica* L. roots extract in Wistar rats was observed by Kodati et al. On the ~~surface of the wound, 10% (w/w) extract ointment was applied to assess the activity of wound healing~~ ~~wound's surface, 10% (w/w) extract ointment was applied to assess the wound healing activity~~. It was discovered that starting on the sixth day, the rats given extract showed a notable improvement in their ability to close wounds. With the extract, there was a ~~greater-more significant~~ percentage of wound contraction and a shorter wound closure time. Furthermore, the groups treated with the extract showed ~~full-complete~~ wound healing in 16 days, while the control group showed epithelization in more than 20 days.<sup>57</sup> *Chitrak's* carminative, anti-inflammatory, expectorant, diuretic, androgenic, analgesic, anti-convulsant, adaptogenic, anti-pyretic, and muscle-relaxant properties make it a popular choice for the treatment and management of digestive disorders. *Chitrak* is a traditional remedy for gastrointestinal disorders that include heartburn, indigestion, diarrhea, flatulence, peptic ulcers, esophagitis, and stomach discomfort. It is also used to support gut health. As a carminative herb, it facilitates the breakdown of food particles in the stomach and intestine, stimulates the flow of digestive juices, and ~~so improves the~~ ~~improves~~ intestinal absorption of essential nutrients. Additionally, ~~by aiding in the expulsion of stomach gas,~~ ~~aiding in the expulsion of stomach gas~~ reduces bloating, abdominal distension, and gastric cramps. Herbal laxatives work by allowing excrement to pass freely from the anus.<sup>58</sup>

**6. Haridra (Turmeric):-***(Curcuma longa Linn.)*:- *Haridra (Curcuma longa Linn)* belongs to the *Zingiberaceae* family. *Rasa* is *Katu, Tikta*, *Guna* is *Laghu, Ruksha Vipaka* is *Katu, Veerya Ushna*.<sup>59</sup> Chemical components of turmeric are named curcuminoids, which include mainly

curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin. Curcumin (diferuloylmethane) is a polyphenol derived from the *Curcuma longa* plant, commonly known as turmeric. The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone. Curcumin works by interacting with the gut microbiota, ~~which is~~ a population of bacteria, fungi, and viruses that live in the intestines of humans and aid with digestion and immunity. During the developmental stage of the fetus, the microbiota begins to colonize. When fully grown, these organisms not only fight infections but also help to regulate metabolism, produce vitamins B and K, and support the growth of the immune system.<sup>60</sup> Turmeric inhibits nuclear factors (NF-~~N.F.~~)-B, which in turn decreases the synthesis of adhesins and inflammatory mediators, hence lessening intestinal damage in cases of induced gastropathy. Following therapy, turmeric reduces mucus damage to the stomach and prevents leukocyte adhesions, ICAM1 sticky proteins, and TNF production. *Curcuma longa* extract pills considerably reduced the incidence of ~~IBS-I.B.S.~~ and the ratings of stomach discomfort throughout ~~the course of~~ eight treatments. Substantial improvements were observed in the ~~IBS-I.B.S.~~ life quality (~~QOL-Q.O.L.~~) measurements. Male mice who have APAP-induced cirrhosis are protected from it by curcumin, which improves liver histology by lowering oxidative stress, decreasing inflammation in the liver, and raising ~~GSH-G.S.H.~~ levels.<sup>61</sup> In rat mesenteric myeloid cells, ~~curcumin-curcumin~~ suppressed degranulation and the adrenaline substance 48/80-induced discharge. Curcumin decreased the chemical that might cause passive cutaneous anaphylactoid response mediated by anti-DNP immunoglobulin E (IgE) in vivo and systemic anaphylaxis in vitro. Curcumin reduces allergic reactions mediated by mast cells, both specific and general. Indian materia medica provides a thorough explanation and documentation of the medical benefits of turmeric, also known as *Haridra*. It helps with ~~IBS-I.B.S.~~ and is regarded as the greatest anti-helminthic for ~~GIT-G.I.T.~~ disorders. ~~The best herb for respiratory issues like rhinitis, bronchitis, sore throats, and coughs is Haridra~~ *Haridra* is the best herb for respiratory issues like rhinitis, bronchitis, sore throats, and coughs. Numerous studies have determined that the most potent anti-inflammatory medication is curcumin.

*Curcuma Longa* rhizome ethanolic extract has a significant hepatoprotective effect when taken orally. Among antioxidants, it ought to be among the best.<sup>62</sup> It is believed that Curcuma oil mitigates nitrosative and oxidative stress, ~~hence~~ shielding against the deleterious consequences of ischemia. The successive induction of apoptosis was significantly inhibited by Curcuma oil. In light of this, research demonstrates the remarkable neuroprotective properties of curcuma oil. Studies on individuals, animals, and cell cultures have all shown that turmeric possesses chemo-preventive qualities. Curcumin is thought to have anti-cancer potential because of its effects on mutations, oncogenic transcription, cell cycle regulation, apoptosis, carcinogenesis, and metastasis. Numerous malignancies have also been found to possess anti-proliferative properties. Curcumin ~~is used to stop~~ ~~stops~~ ~~both~~ the passive cutaneous anaphylactoid reaction caused by anti-DNP immunoglobulin E (IgE) in vivo and global anaphylaxis in vitro. One potent inhibitor of drug resistance is curcumin. It possesses a ~~special-remarkable~~ ability to prevent the upregulation of P-glycoprotein's mRNA. Curcumin has a well-established synergistic anti-cancer effect. In West Bengal, Uttar Pradesh, and Bihar, ~~the rhizome of Curcuma longa is used traditionally~~ *Curcuma longa's rhizome is traditionally used* to treat

coughs, colds, and loose stools. The benefits of *Haridra* as a therapeutic and prophylactic treatment are well-known worldwide.<sup>63</sup>

## DISCUSSION

In celiac disease, the small intestine's inner lining is damaged by an immune reaction, which stops it from absorbing nutrition. This disorder is known as malabsorption. Growth and development are delayed in children with celiac disease. When persons with celiac disease ingest gluten-rich foods, their immune systems respond to it. (The protein known as gluten is found in wheat, rye, oats, and barley.) Symptoms such as severe stomach pain and discomfort, digestive discomfort, and diarrhoea occurs which results in inflammation in the small intestine. The response damages the villi of the small intestine. Villi are responsible for absorbing vitamins and minerals. Insufficient nutrients might be absorbed by the body. The body might absorb insufficient nutrients if these villi are destroyed. According to *Ayurveda*, this illness denotes a *Dosha* imbalance in the body that weakens the immune system and digestion. Poor food and lifestyle choices weaken immunity by vitiating *Pitta* and *Vata* in the gut. The digestive system is too sensitive, which results in an allergic response to some gluten-containing meals. It causes food malabsorption, which can result in loose stools, weight loss, etc. In *Ayurveda*, this is referred to as celiac disease. Digestive problems in children with celiac disease are more common than in adults and might include nausea and vomiting, persistent diarrhoea, abdominal discomfort, constipation, gas, pale, offensive faeces, etc. According to *Ayurveda*, this can correlate with *Grahani Dosha* in *Ayurveda*. *Grahani* is described as an *Agni Adhithana* by most of *Acharya*. *Mandagini* is a root cause of *Ama Dosha*, and it is a crucial factor for manifestation of the most diseases' manifestation-most of diseases. Among them is the prime disease of the gastrointestinal tract-gastrointestinal tract disease which is seen oft, which is often seen. The management approach of celiac disease in *Ayurveda* proceeds with the adoption of *Sanshodhan-Vidhi* (emesis/Purgation), and it is complemented by the use of palliative medicines-the use of palliative medicines complements it. These therapeutic plants for certain illnesses aid in restoring a regular digestive fire and expelling "*Ama*" poisons from the body's channels. Thus, this line of *Ayurveda* treatment approaches through the intake of medicinal plants helps in the complete reversal of-completely reverse the condition and enables holistic health benefits. In the management of celiac disease, Some *Ayurvedic* herbs like *Kutaja*, *Pippali*, *Chitaka*, *Guduchi*, *Ashwagandha*, *Haridra*, etc. are found effective to manage in managing this disease, which have-has *Agni Deepana* and *Aam Pachana* and anti-inflammatory properties. These illness-specific medicinal herbs help in the normalization of digestive fire and evicting-normalize digestive fire and evict "*Ama*" toxins from the body channels. *Kutaj* has anti-inflammatory, anti-dysenteric properties and also anti-dysenteric properties and inhibits goblet cell rupture, cellular infiltration, and mucosal layer inflammation.<sup>64</sup> *Pippali* has anti-inflammatory, antioxidant, and anti-ulcer properties, and the inhibitory effect of piperine on stomach emptying occurs independently of the release of gastric acid and pepsin.<sup>65</sup> *Chitraka* has carminative, anti-inflammatory, diuretic, androgenic, analgesic, adaptogenic, anti-pyretic, and muscle-relaxant properties making it a popular choice for the treatment and management of digestive disorders.<sup>66</sup> As a carminative herb, it facilitates the breakdown of food particles in the stomach and intestine, stimulates the flow of digestive juices, and so improves the intestinal absorption of essential nutrients. Additionally, by aiding in the expulsion of stomach gas, it aiding in the expulsion of stomach gas reduces bloating, abdominal distension, and gastric cramps. Herbal laxatives work by allowing excrement to pass

freely from the anus. *Guduchi* has anti-inflammatory, antiviral, antipyretic, and wound-healing properties. <sup>67</sup> *Ashwagandha* has shown promising immunomodulating as well as antibacterial and anti-inflammatory properties, anti-oxidant, anxiolytic, and adaptogen properties. <sup>68</sup> *Haridra* has anti-inflammatory, anti-diarrhoeal, hepatoprotective, and antioxidant properties. <sup>69</sup> These herbal drugs are used for the management of celiac disease.

#### CONCLUSION:

Celiac disease is a lifelong multi-systemic disease triggered by intake of gluten in genetically susceptible individuals. It is determined from the above description that *Annavaha Srotas-Dusti* vitiation causes celiac disease. As a result, such herbs and ~~herb~~herbal-mineral formulations are needed, which may ~~both~~ reduce celiac disease pathogenesis and create homeostasis among vitiated *Doshas*. Several experimental and clinical research established that *Kutaja*, *Pippali*, *Chitaka*, *Guduchi*, *Ashwagandha*, and *Haridra* are useful herbs in treating celiac disease, which ~~are~~ are quite safe, cheaper, and risk-free.

#### REFERENCE:-

1. Husby, S., Koletzko, S., Korponay-Szabó, I., Kurppa, K., Mearin, M. L., Ribes-Koninckx, C., Shamir, R., Troncone, R., Auricchio, R., Castillejo, G., Christensen, R., Dolinsek, J., Gillett, P., Hróbjartsson, A., Koltai, T., Maki, M., Nielsen, S. M., Popp, A., Størdal, K., Werkstetter, K., ... Wessels, M. (2020). European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. *Journal of pediatric gastroenterology and nutrition*, 70(1), 141–156. <https://doi.org/10.1097/MPG.0000000000002497> [PubMed]
2. Fasano, A., & Catassi, C. (2012). Clinical practice. Celiac disease. *The New England journal of medicine*, 367(25), 2419–2426. <https://doi.org/10.1056/NEJMcpl113994> [PubMed]
3. Robert M Kliegman, Joseph St (2020) Nelson text Book of Pediatrics, 21st Edition, volume 2, Geme Philadelphia, Elsevier1991
4. Tye-Din, J. A., Galipeau, H. J., & Agardh, D. (2018). Celiac Disease: A Review of Current Concepts in Pathogenesis, Prevention, and Novel Therapies. *Frontiers in pediatrics*, 6, 350. <https://doi.org/10.3389/fped.2018.00350>
5. Savvateeva, L. V., Erdes, S. I., Antishin, A. S., & Zamyatnin, A. A., Jr (2018). Current Paediatric Coeliac Disease Screening Strategies and Relevance of Questionnaire Survey. *International archives of allergy and immunology*, 177(4), 370–380. <https://doi.org/10.1159/000491496> [PubMed]
6. McAllister, B. P., Williams, E., & Clarke, K. (2019). A Comprehensive Review of Celiac Disease/Gluten-Sensitive Enteropathies. *Clinical reviews in allergy & immunology*, 57(2), 226–243. <https://doi.org/10.1007/s12016-018-8691-2> [PubMed]
7. Caio, G., Volta, U., Sapone, A., Leffler, D. A., De Giorgio, R., Catassi, C., & Fasano, A. (2019). Celiac disease: a comprehensive current review. *BMC medicine*, 17(1), 142. <https://doi.org/10.1186/s12916-019-1380-z>

Formatted: Portuguese (Brazil)

8. Bai, J. C., & Ciacci, C. (2017). World Gastroenterology Organisation Global Guidelines: Celiac Disease February 2017. *Journal of Clinical Gastroenterology*, 51(9), 755–768. <https://doi.org/10.1097/MCG.0000000000000919>

Formatted: Portuguese (Brazil)

9. Walker, M. M., Ludvigsson, J. F., & Sanders, D. S. (2017). Coeliac disease: review of diagnosis and management. *The Medical Journal of Australia*, 207(4), 173–178. <https://doi.org/10.5694/mja16.00788>. [PubMed]

10. Do Vale, R. R., Conci, N. D. S., Santana, A. P., Pereira, M. B., Menezes, N. Y. H., Takayasu, V., Laborda, L. S., & da Silva, A. S. F. (2018). Celiac Crisis: an unusual presentation of gluten-sensitive enteropathy. *Autopsy & case reports*, 8(3), e2018027. <https://doi.org/10.4322/acr.2018.027>. [PubMed]

11. Yadavji T., Charak Samhita on Ayurved Dipika commentary by Agnivesh, published by Chowkhamba Krishnadas Academy, Varanasi, edition- reprint 2015, Chikitsa Sthana, Chapter-15, p.517

12. Yadavji T, Sushruta Samhita on Nibandha Sangraha commentary by Dalhan, Published by Chaukhamba Sanskrit Sansthan, Varanasi, Edition Reprint 2012, Uttar tantra, Chapter -40, p. 709.

13. Swami D. and DR. M.L. Gharote Copyright 1978 by: Kaivalyadhama S.M.Y.M. Samiti, Lonavla (Maharashtra-India) – 410- 403 First published Mahashivaratri, 7th 1 March, 1978 Second Edition April 1997)

14. Pt. Shastri H. S.P . Ashtanga Hridayam ,with sarvangasundara and Ayurved Rasayana Commentry by Arundutta and Hemadri respectively .Nidanasathana , Atisaragrahani Adhyaya 89 , Chaukhamba Surbharati Prakashana; , Varanasi 2002, page no. 498-499.

15. S.Muktibodhanand, Hatha yoga Pradipika-a light on hatha yoga, Yoga Publications Trust, Munger, Bihar India (199)

16. Jain, Sapan & Chawardol, Seema & Jain, Jinesh & Dwivedi, O.P. (2018). Management of Grahani Roga by Ayurveda principles and life style modification. *Journal of Drug Delivery and Therapeutics*. 8. 393-396. 10.22270/jddt.v8i6.2061.

17. Yadav, Parag. (2020). Medical Perspective on Ama as per Ayurveda and Modern Consideration: A Review. *Journal of Drug Delivery and Therapeutics*. 10. 205-207. 10.22270/jddt.v10i1-s.3861.

18. Chunekar KC. *Bhavaprakasha Nighantu (Indian materia medica)*; Chaukhambha Bharati Academy, Varanasi. reprint 2018:257-465

19. Kumar, A., & Ali, M. (2000). A new steroidal alkaloid from the seeds of *Holarrhena antidysenterica*. *Fitoterapia*, 71(2), 101–104. [https://doi.org/10.1016/s0367-326x\(99\)00111-2](https://doi.org/10.1016/s0367-326x(99)00111-2)

Formatted: Portuguese (Brazil)

Formatted: No underline, Font color: Auto, Portuguese (Brazil)

Formatted: Portuguese (Brazil)

Formatted: Portuguese (Brazil)

Field Code Changed

Formatted: Portuguese (Brazil)

Formatted: Portuguese (Brazil)

Formatted: No underline, Font color: Auto, Portuguese (Brazil)

Formatted: Portuguese (Brazil)

Formatted: French (France)

Formatted: French (France)

Field Code Changed

Formatted: French (France)

Formatted: French (France)

20. Yang, Z. D., Duan, D. Z., Xue, W. W., Yao, X. J., & Li, S. (2012). Steroidal alkaloids from *Holarrhena antidysenterica* as acetylcholinesterase inhibitors and the investigation for structure-activity relationships. *Life Sciences*, 90(23-24), 929–933. <https://doi.org/10.1016/j.lfs.2012.04.017>

21. Ganapathy, Sujana & Ramachandra, Y L & Rai, Padmalatha. (2011). Anti-inflammatory and analgesic activities of *Holarrhena antidysenterica* Wall. Leaf extract in experimental animal models. 4. 101-103.

Formatted: No underline, Font color: Auto, French (France)

Formatted: French (France)

22. Shwetha C, Latha KP, Asha K. Study on analgesic activity of *Holarrhena antidysenterica* leaves. International Journal of Herbal Medicine. 2014; 2(3): 14-1 Anti-diarrhoeal activity

Formatted: Font: Italic

23. Sharma DK, Gupta VK, Kumar S. Evaluation of anti-diarrheal activity of ethanolic extract of *Holarrhena antidysenterica* seeds in rats. Veterinary World. 2015; 8(4): 1392-1395.

24. Kunal, Gupta & Karale, Sanjiv & Vijayanand, Warad. (2012). Anti diarrhoeal activity of a polyherbal formulation in various animal models diarrhoea. International Research Journal of Pharmacy. 3. 289-290.

25. Chuneekar, K.C., Bhavaprakash Nighantu, 6th edition, Chaukhambha Bharat Academy, Varanasi, 1982) page no.-15.

26. Kumari, Mamta & Bk, Ashok & Ravishankar, Basavaiah & Pandya, Tarulata & Acharya, Rabinarayan. (2012). Anti-inflammatory activity of two varieties of Pippali (*Piper longum* Linn.). Ayu. 33. 307-10. 10.4103/0974-8520.105258.

27. Database on Medicinal Plants Used in Ayurveda, by PC Sharma, MB Yelne and TJ Dennis, Central Council For Research In Ayurveda & Siddha, Reprint Janakpuri, New Delhi, Part I, 2005; II(3):472)

28. Sharma A and Singh R. Screening of anti-inflammatory activity of certain indigenous drugs on carrageenin induced hind paw edema in rats, Bull. Med. Ethnobot. Res 1980; 2:262)

29. Kumar S, Arya P, Mukherjee C, Singh BK, Singh N, Parmar VS. Novel aromatic ester from *Piper longum* and its analogues inhibit expression of cell adhesion molecules on endothelial cells. Biochemistry 2005;6;44:15944-52.

30. Choudhary GP. Mast cell stabilizing activity of piper longum Linn. Indian J Allergy Asthma Immunol 2006;20:112-6.

31. Stöhr, J. R., Xiao, P. G., & Bauer, R. (2001). Constituents of Chinese *Piper* species and their inhibitory activity on prostaglandin and leukotriene biosynthesis in vitro. *Journal of Ethnopharmacology*, 75(2-3), 133-139. [https://doi.org/10.1016/S0378-8741\(00\)00397-4](https://doi.org/10.1016/S0378-8741(00)00397-4)

32. Natarajan, K.S., Narasimhan, M., Radha, S.K. and Shanmugasundaram, E.R.B. (2006) Antioxidant Activity of a Salt-Spice-Herbal Mixture against Free Radical Induction. *Journal of Ethnopharmacology*, 105, 76-83. <https://doi.org/10.1016/j.jep.2005.09.043>

33. Vedhanayaki, G., Shastri, G. V., & Kuruvilla, A. (2003). Analgesic activity of *Piper longum* Linn. root. *Indian journal of experimental biology*, 41(6), 649-651.

34. Bajad S, Bedi KL, Singla AK, Johri RK. Piperine inhibits gastric emptying and gastrointestinal transit in rats and mice. *Planta Med*. 2001;67(2):176-179. doi:10.1055/s-2001-11505

35. Dhanush SS, Lakshmi SP, Prakash L. Hegde. A Review of Vrushya Dravyas of Guduchyadi Varga of Bhavaprakasha Nighantu.- J Ayurveda Integr Med Sci 2021;3:46-49.
37. The Ayurvedic Pharmacopoeia of India, Part-I, Volume- I, Government of India, Ministry of Health and Family Welfare, Department of Ayurveda, Yoga, Naturopathy, Unani, Siddha & Homeopathy, New Delhi. From: <http://www.ayurveda.hu/api/API-Vol-1.pdf>
38. Bafna, P. A., & Balaraman, R. (2005). Anti-ulcer and anti-oxidant activity of pepticare, a herbomineral formulation. *Phytomedicine : international journal of phytotherapy and phytopharmacology*, 12(4), 264–270. <https://doi.org/10.1016/j.phymed.2003.12.009>[Pub Med]
39. Mohan H. Textbook of Pathology. 5th ed., New Delhi: Jaypee Brothers Medical Publisher (P) Ltd., 2010; 6: 133.
40. Patgiri, B., Umretia, B., Vaishnav, P., Prajapati, P., Shukla, V., & Ravishankar, B. Anti-inflammatory activity of Guduchi Ghana (aqueous extract of *Tinospora cordifolia* Miers.). *AYU (An International Quarterly Journal of Research in Ayurveda)*, 2014; 35(1): 108. <https://doi.org/10.4103/0974-8520.141958>.
41. Antonisamy P, Dhanasekaran M, Ignacimuthu S, Duraipandiyan V, Balthazar JD, Agastian P, et al. Gastroprotective effect of epoxyclerodane diterpene isolated from *Tinospora cordifolia* Miers (Guduchi) on indomethacin-induced gastric ulcer in rats. *Phytomedicine* 2014; 21(7): 966-969. doi:10.1016/j.phymed.2014.02.010
42. Sarma ~~DNK~~D.N.K., Khosa RL, Chansauria ~~JPN~~J.P.N., Sahai M. Antiulcer activity of *Tinospora cordifolia* miers and *Centella asiatica* Linn extracts. *Phytother Res* 1995; 9: 589-90.
43. Alexander CP, Kirubakaran CJ, Michael RD. Water soluble fraction of *Tinospora cordifolia* leaves enhanced the non-specific immune mechanisms and disease resistance in *Oreochromis mossambicus*. *Fish Shellfish Immunol*. 2010;29(5):765-772. doi:10.1016/j.fsi.2010.07.003
44. Sharma P.V, Dravya GunaVigyana, Chaukhambha Bharati Academy, Varanasi, Reprint 2003;(2)
45. Kulkarni, S. K., & Dhir, A. (2008). *Withania somnifera*: an Indian ginseng. *Progress in neuro-psychopharmacology & biological psychiatry*, 32(5), 1093–1105. <https://doi.org/10.1016/j.pnpbp.2007.09.011>
46. Saleem, S., Muhammad, G., Hussain, M. A., Altaf, M., & Bukhari, S. N. A. (2020). *Withania somnifera* L.: Insights into the phytochemical profile, therapeutic potential, clinical trials, and future prospective. *Iranian journal of basic medical sciences*, 23(12), 1501–1526. <https://doi.org/10.22038/IJBMS.2020.44254.10378>
47. Kanji lal S., Gupta A.K., Patnaik R.S., Dey A. Analysis of Clinical Trial Registry of India for Evidence of Anti-Arthritic Properties of *Withania somnifera* (Ashwagandha) *Altern. Ther. Health Med*. 2021;27:58–66. [PubMed] [Google Scholar]

Formatted: Portuguese (Brazil)

Field Code Changed

Formatted: Portuguese (Brazil)

Formatted: Portuguese (Brazil)

48. Dar, N. J., Hamid, A., & Ahmad, M. (2015). Pharmacologic overview of *Withania somnifera*, the Indian Ginseng. *Cellular and molecular life sciences*: [CMLS.C.M.L.S.](#), 72(23), 4445–4460. <https://doi.org/10.1007/s00018-015-2012-1>

49. Davis, L., & Kuttan, G. (2000). Immunomodulatory activity of *Withania somnifera*. *Journal of Ethnopharmacology*, 71(1-2), 193–200. [https://doi.org/10.1016/s0378-8741\(99\)00206-8](https://doi.org/10.1016/s0378-8741(99)00206-8)

50. Mandlik Ingawale, D. S., & Namdeo, A. G. (2021). Pharmacological evaluation of Ashwagandha highlighting its healthcare claims, safety, and toxicity aspects. *Journal of dietary supplements*, 18(2), 183–226. <https://doi.org/10.1080/19390211.2020.1741484>

51. Rawat, Neha & Roushan, Rakesh. (2019). Ashwagandha (*Withania Somnifera*): A potential aphrodisiac drug in Ayurveda. 8. 1034-1041.

52. Bhavamishra, Bhavaprakasha Nighantu Commentary by Chunekar Krishnachandra, Edited by Pandey Gangasahaya, Chaukambha Bharati Academy, Varanasi, Reprint 1999.

53. Shukla, B., Saxena, S., Usmani, S. *et al.* Phytochemistry and pharmacological studies of *Plumbago zeylanica* L.: a medicinal plant review. *Clin Phytosci* 7, 34 (2021). <https://doi.org/10.1186/s40816-021-00271-7>

54. Sheeja E, Joshi SB, Jain DC. Bioassay-guided isolation of anti-inflammatory and antinociceptive compound from *Plumbago zeylanica* leaf. *Pharm Biol.*2010;48(4):381–7. <https://doi.org/10.3109/13880200903156424>

55. Subramaniyan V, Paramasivam V. Potential anti-inflammatory activity of *Plumbago zeylanica*. *Asian J Pharm Clin Res.* 2017;10(10):372–5. <https://doi.org/10.22159/ajpcr.2017.v10i10.20357>

56. Falang KD, Uguru MO, Wannang NN, Azi IH, Chiamaka N. Antiulcer activity of *Plumbago zeylanica* Linn root extract. *J Nut Prod Plant Resour.* 2012;2(5):563–7

57. Kodati, Devender & Burra, Shashidher & P, Kumar. (2011). Evaluation of Wound healing activity of methanolic root extract of *Plumbago zeylanica* L. in [wistar-Wistar](#) albino rats. *Asian Journal of Plant Science and Research.* 1. 26-34.

58. Choudhary, Shailja & Kaurav, Hemlata & Chaudhary, Gitika. (2021). Chitraka (*Plumbago zeylanica*): A Potential Rejuvenator. *International Journal for Research in Applied Sciences and Biotechnology.* 8. 202-212. 10.31033/ijrasb.8.2.26.

59. Bhavmisra Bhavaprakasha Nighantu (edited by Dr. G.S. Pandey, commentary by Dr. K.C. Chunekar), *Haritakyadi Varga/197*, reprint, published by Chaukambha Bharti Academy, Varanasi, 2009; 114.

60. Scazzocchio, B., Minghetti, L., & D'Archivio, M. (2020). Interaction between Gut Microbiota and Curcumin: A New Key of Understanding for the Health Effects of Curcumin. *Nutrients*, 12(9), 2499. <https://doi.org/10.3390/nu12092499>

61. S. A, H. A, and H. P. L, "Pharmacological activities of wild turmeric (*Curcuma aromatic Salisb*): a review," *J. Pharmacogn. Phytochem.*, 2015

Formatted: French (France)

Formatted: French (France)

62. Duggi, Shrishail & Handral, Harish & Handral, Ravichandra & G, Tulsianand & ~~SDS.D.~~, Dr. Shruthi. (2013). Turmeric: ~~Nature's~~ Nature's precious medicine. Asian Journal of Pharmaceutical and Clinical Research. 6. 10-16.
63. Rao C. V. (2007). Regulation of COX and ~~LOX~~ L.O.X. by curcumin. *Advances in experimental medicine and biology*, 595, 213–226. [https://doi.org/10.1007/978-0-387-46401-5\\_9](https://doi.org/10.1007/978-0-387-46401-5_9)
64. Gopinath, G & Margesan, M. Thirumal & Kumar, P. (2020). Holarrhena antidysenterica Linn. – A Review. Research Journal of Pharmacy and Technology. 13. 2013. 10.5958/0974-360X.2020.00362.5.
65. Warriar PK, Nambiar VP, Raman KC. Vol. 4. Madras, India: Orient Longman Ltd; 1995. *Piper longum*, Indian ~~M~~medicinal Plants. p. 290. [Google Scholar]
66. Dr. Mulker V. G. and Dr. Ghotankar A. M. Therapeutic Uses Of Chitraka (Plumbago Zeylanica Linn.) With a Note On ~~It's~~ Its Pharmacological Actions. -A REVIEW, ~~WJPMR~~ wjpmr, 2020,6(4), 56-59
67. Rawat, Neha & Roushan, Rakesh. (2018). Guduchi; A Potential Drug In Ayurveda. 7. 355-361. 10.20959/wjpr201812-12674
68. Khanchandani, Nisha & Shah, Prachi & Kalwani, Twinkle & Ardesna, Anujkumar & Dharajiya, Darshan. (2019). Antibacterial and Antifungal Activity of Ashwagandha (Withania somnifera L.): A Review. 9. 154-161. 10.22270/jddt.v9i5-s.3573.
69. Chakraborty S. & Das A. A Classical Ayurveda Review On Haridra. *Ayushdhara*, 7(Supply1),47-55.(2020) <https://doi.org/10.47070/ayushdhara.v7iSupply1.579>

Formatted: Portuguese (Brazil)