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Review Paper

Beyond Gluten Free: A Systematic Review of Botanical Intervention in Celiac Disease Symptoms Management

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ABSTRACT

Celiac disease is a chronic immune mediated disorder which triggered by gluten ingestion in genetically susceptible individuals. Most commonly of those individuals carrying the HLA DQ2 or HLA DQ8 haplotypes. Despite its worldwide prevalence and rising incidence where the condition often remains undiagnosed because of its wide spectrum of gastrointestinal, extraintestinal and autoimmune manifestations. Conventional diagnosis depend on small intestinal biopsy and serological markers such as anti tTG and anti endomysial antibodies but non-biopsy approaches are increasingly accepted in pediatric populations with the strongly positive serology. While strict lifelong adherence to gluten free diet remains the keystone of therapy. The limitations of dietary management and symptom which burden in many patients lifestyle so need for complementary therapeutic strategies. This review explores the emerging role of medicinal plants in the symptomatic management of celiac disease. Three herbs Aegle marmelos (Bael), Eclipta alba (Bringraj) and Convolvulus pluricaulis (Shankhpushpi) are observed for their rich in phytochemicals and pharmacological properties. These plants contains many phytochemicals such as alkaloids, flavonoids, tannins, coumestans, terpenoids and phenolics which shows anti inflammatory, antioxidant, immuno modulatory, gastroprotective and also neuroprotective properties. Evidence suggests that these herbal agents may support the gut integrity, reduces the oxidative stress, modulate the immune responses and alleviate digestive and also the systemic symptoms which commonly associated with celiac disease. Even though more clinical studies are needed, current evidence suggests that certain herbal treatments can support the gluten-free diet and help improve patient comfort and quality of life.

INTRODUCTION

Celiac disease in children and celiac sprue in adults are likely the same condition with an

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identical underlying mechanism. The alternate names includes Coeliac disease (British usage), Celiac sprue, Nontropical sprue, Gluten-sensitive enteropathy and Idiopathic steatorrhea [1]. Celiac disease is an immune mediated systemic disease condition triggered by consuming gluten and related prolamins in individuals with genetic susceptibility. It is seen by various combinations of injury to the small intestine and the presence of celiac specific antibodies like human leukocyte antigen HLA DQ2 or HLA DQ8 and also clinical symptoms that depend on gluten exposure [2]. Although approximately 90%–95% of individuals with celiac disease (CD) carry the HLA-DQ2 haplotype and to the surprise most of the remaining patients carry HLA-DQ8 but These genetic markers alone do not guarantee the development of the disease. This is because up to 30%–40% of the general population, who do not have CD, also possess these markers. This suggests that other environmental influences and immune system factors play essential roles in triggering the start of the disease [3]. Since gluten was identified as the factor for celiac disease (CD) in the 1950s. A strict and lifelong gluten free diet (GFD) has remained the cornerstone of management. Although Celiac disease is prevalent worldwide and its incidence is increasing in world wide many populations, it often goes unrecognized and undiagnosed in clinical settings [4]. Over recent decades, the worldwide occurrence of this disease has increased, now affecting about 1% of people globally [5]. Initially, the diagnosis relied solely on identifying typical gastrointestinal symptoms. Awareness of the disease significantly increased in the 1960s with the introduction of

more specific tests for malabsorption and the development of the pediatric peroral biopsy technique. As a result, studies from Ireland, Scotland, and Switzerland reported a rise in disease incidence, reaching a peak of approximately 1 in 450 individuals by the mid-1970s [6]. Specialists consider celiac disease (CD) to be on a delicate balance between the over diagnosed and underdiagnosed. This situation occurs mainly because atypical forms of celiac disease which are often as common or even more frequent than the classic symptoms which is contribute to diagnostic challenges to specialists [7]. Current diagnostic criteria for celiac disease is depends on identifying enteropathy in small intestinal biopsies. Histological examination shows villous atrophy and crypt hyperplasia and also increased intraepithelial lymphocytes. Additionally diagnosis is supported by the detection of circulating celiac disease specific antibodies opposed to tissue trans glutaminase and deamidated gliadin peptides and also endomysium. In pediatric patients (children who are affected) exhibiting symptoms indicative of CD. Diagnosis may be established without biopsy if there is a strongly elevated tG antibody (tTGA) level which combined with the presence of CD associated HLA genotypes. This non-biopsy approach is increasingly accepted, particularly in cases with highly positive serology and compatible genetics, improving diagnostic efficiency and reducing invasive procedures [8].

1.1 Key factors influencing the development of celiac disease



Table 1: Key factors influencing the development of celiac disease [9].

Factor	Strong Evidence	Limited or Uncertain Evidence
Gluten	Essential trigger for the disease	
Genetics	Requires HLA DQ2 or DQ8; twin studies confirm risk; chromosomal increase susceptibility	Over 40 additional genes, each contributing minimally; higher prevalence in females
Infant Nutrition	Amount of gluten consumed	Breastfeeding under age 2 may lower risk
Pregnancy & Birth Circumstances	Low birth weight increases risk	C section delivery (inconsistent finding); birth season; maternal iron supplementation
Area	Living in northern, wheat producing areas (e.g., northern US) linked to higher rates	White racial background
Infections & Gut Health	Reovirus infection, other infection and antibiotic use are associated	Imbalanced gut bacteria, poor oral health, influenza, absence of Helicobacter, rotavirus
Socioeconomic Status & Smoking	Smoking is negatively associated with celiac disease	Wealthier background, no impact of maternal smoking, higher maternal education

1.2 Clinical Manifestation

- Gastrointestinal Symptoms
 - a. Irritable bowel syndrome like symptoms
 - b. Diarrhea
 - c. Heartburn
 - d. Altered bowel habits
 - e. Bloating
 - f. cow's milk intolerance
- Extraintestinal presentations
 - a. Dermatitis herpetiformis
 - b. Alopecia areata
 - c. Vitiligo
 - d. Dermatomyositis
 - e. Osteopenic bone disease
 - f. Iron deficiency
 - g. Chronic fatigue
 - h. Folate deficiency
 - i. Neuropsychiatric manifestations
 - j. Gluten ataxia
 - k. Peripheral neuropathies
 - l. Infertility

m. Low birth weight

- Autoimmune endocrine disorders
 - a. Type 1 diabetes
 - b. Autoimmune thyroid disease
 - c. Addison's disease
 - d. Autoimmune adrenal disease
- Autoimmune connectivetissue disorders
 - a. Sjogren's syndrome
 - b. Rheumatoid arthritis
 - c. lupus erythematosus
- Liver diseases
 - a. Primary biliary cirrhosis
 - b. Autoimmune hepatitis
 - c. Primary sclerosing hepatitis
 - d. Elevated amino transferase levels
- Miscellaneous conditions
 - a. IgA deficiency
 - b. IgA nephropathy
 - c. Down syndrome
 - d. Turner's syndrome



- Cardiological diseases
 - a. Dilated cardiomyopathy
 - b. Autoimmune pericarditis
- Other
 - a. Psoriasis
 - b. Pancreatitis
 - c. Enteropathy T cell lymphoma
 - d. Immune thrombo cytopenic purpura
 - e. AIDS
 - f. Crohn's disease of the small intestine
 - g. Carbohydrate intolerance
 - h. Short stature
 - i. Dental enamel defects

Signs and symptoms of celiac disease observed in affected individuals, including several rare manifestations that have been reported in previous research studies [10, 11, 12, 13, 14].

The reasons why celiac disease develops in certain population remain unclear. Epidemiology and prospective studies refers various environmental factors which can influence celiac disease onset. Emerging evidence also highlights the part of microbiome in shaping immune tolerance and which also contributing to pathogenesis of disease. Genetic and immunologic research has identified critical HLA and non HLA susceptibility genes participating in celiac disease along with a persistent population of gluten specific T cells which identify particular gluten peptides (T cell epitopes). The current understanding of celiac disease indicates the environmental factors influence disease risk in genetically predisposed individuals by the modifying the immune environment where gluten is presented tipping the balance from the gluten tolerance toward immune reactivity. This process may be partially determined by interactions between the microbiome and host immune system. Important clinical priorities include accelerating CD detection and diagnosis which direction the enhancing quality of life and health outcomes for

patients and developing more effective and less burdensome treatments beyond the lifelong strict gluten free diet [15]. This review explores the emerging role of herbal and botanical therapies as novel symptomatic management options for celiac disease, highlighting the anti-inflammatory, immunomodulatory and gut-healing properties of various medicinal herbs which show potential in alleviating gastrointestinal symptoms and enhancing the quality of life for affected individuals beyond the conventional gluten free diet.

2. PLANT PROFILE SHOWING THE SYMPTOMATIC MANAGEMENT OF THE CD:

2.1 Aegle marmelos (Beal)



FIGURE: Aegle marmelos

2.1.1 Taxonomical Classification of A.marmelos [16,21]

kingdom	Plantae
Sub kingdom	Tracheobionta
Super division	Spermatophyta
Class	Magnoliophyta
Sub class	Magnoliopsida
Order	Sapindales
Family	Rutaceae
Sub family	Aurantioideae
Genus	Aegle
species	A.marmelos

2.1.2 Vernacular names of *A.marmelos*[17]

Languages	Names
Hindi	Bel, Bela, Bel patra, Shriphal
English	Bael fruit tree, Bael tree, ball tree, bela tree, elephant apple, golden apple, holy fruit, quince apple of India, stone apple, wood apple
Sanskrit	Bilva, Bilvam, Bilva phalam, Mahura, Shivaphala, Shivadruma, Shaelpatra, Lakshmiputra, Shivestha
Gujarati	Bel, Bilivaohal, Billi
Urdu	Bel, Bael
Bengali	Bael, Bela, Shriphal
Kannada	Bilpatra, Malura, Kumbala
Marathi	Bela, Kaveeth
Malayalam	Baela koovalam, Kuvalam, Maaredy, Vilvam
Tamil	Bilva, Bilubam, Kuuviram, Villuvam, Vilvam, Vilvama, Vilva-maram, Vilva-pazham
Telegu	Bilva, Bilvamu, Bilva pandu, Maradupandu, Malu remu chettu
Chinese	Mu ju, Yin du gou qi, Ying pi ju
French	Coing de l'Inde, Oranger de Malabar
German	Bengalische quitte, Indische quitte
Japanese	Berunoki, Igure marumerozu
Nepali	Belapatra, Belpatra
Turkish	Hind ayva agh
Spanish	Bela, Milva
Italian	Cotogno d'India

2.1.3 Botanical Description [17-19]

Bael is a spiny tree growing sluggishly with a height of 12–15 m and 90–120 cm in diameter. A moderate sized slender, aromatic tree 6 – 7.5 m with a somewhat fluted ble of 3 – 4.5 m. The trunk of the Bael is a short with soft flaking and also thick bark. Branches armed with straight a sharp axillary thorns 2.5 cm long. Bael inflorescence is formed of tiny 4-7 fragrant flowers which appear along the young branchlets having 4 recurved fleshy petals which are yellowish inside and greenish outside.

Leaves: Leaves of Bael tree are 4-10 cm long, 2-5 cm wide, alternate deciduous, pointed and pinnate or ternate with a long petiole. The leaves are thick, smooth, shining and green or dark green colored with aromatic smell. The young emerging foliage exhibits a pinkish maroon hue and a shiny texture.

Flower: The flowers are supported by stalks, upright which approximately 2 cm in diameter and are arranged and also exude a sweet fragrance. They appears either in the leaf axils or as terminal cymes. Each flower features five shallow, short calyces with broad and the pubescent teeth. The ovary is ovoid to oblong, tapering into a thick,

short style while the stigma is capitate and the number of stamens exceeds 50.

Fruit: The bael fruit is almost smooth, light yellow, brown or cherry red in colour, very hard and turns stony when dry (hence the name given wood apple). Bael fruits are 5-20 cm in diameter of varying sizes and round, ovoid, oblong or pyriform in a shape. The pulp of fruit have brownish-red colored firm with 12 stony carpels which containing one or more hairy seeds. The cavity between the carpel and surrounding seed contains a reddish-brown colored with transparent gluten-like or gummy resinous mass that becomes hard after drying. The fruit pulp is sweet or astringent having an agreeable aromatic odor.

Seed: The number of seeds varies from 10–50. Each seed measures about 1 cm in length and exhibits a flattened and oblong form. Additionally, the seeds are covered with woolly hairs and are enclosed within a sac of sticky, transparent mucilage or gum which solidifies upon drying.

2.1.4 Geographical Description

India is the largest producer of medicinal plants which shows the pharmacological activity around the world so it is mentioned as the Botanical Garden of the World. The bael tree is widely distributed across the country. bael is cultivated across the numerous states in india including Assam, Bihar, Gujarat, Haryana, Himachal Pradesh, Jammu and Kashmir, Punjab, Uttarakhand, Uttar Pradesh, Rajasthan, Madhya Pradesh, Maharashtra, Chhattisgarh, Jharkhand, West Bengal, Andhra Pradesh, Karnataka, Kerala, Tamil Nadu and the Andaman Islands [17,20].

2.1.5 Phytochemical Constituents of Bael

The pulp of the bael fruit is rich in bioactive substances such as alkaloids, carotenoids, phenolics, pectins, tannins, coumarins, flavonoids, and terpenoids, saponins and glycosides according

to studies. Methanol and water are the best solvents for extraction of the metabolites of this plant which followed by the use of ethanol. The phytochemistry of *A. marmelos* has been extensively studied and the plant has been found to contain a variety of biologically active compounds.

Alkaloids: Alkaloids are nitrogen containing compounds which found in verity of plants and recognize for their pharmacological activity. Several alkaloids have been identified in the leaves and roots of *A. marmelos* species including marmesin, marmelosin and aegeline.

Tannins: Tannins are a group of the compounds which widely dispersed in the plant kingdom and also known for their astringent and antioxidant properties. The fruit of *A. marmelos* contains high levels of tannins such as Alanine, Phenyl alanine, Tyrosine, leucine and Iso leucine which have been shown to have strong antioxidant and anti-inflammatory activities.

Flavonoids: Flavonoids are a group of compounds that are widely distributed in the plant kingdom and are known for their anti-inflammatory, anti-cancer and antioxidant activities. Flavonoids are shown in part of plant like in the leaves and roots such as Quercetin, Rutin, Catechin, Flavan-3-ol and also some of these compounds have been shown to have anti nociceptive and antipyretic activities.

Terpenoids: Terpenoids are a group of compounds that are widely dispersed in the plant kingdom and are also known for their medicinal properties. Terpenoids such as Isoterpinene, Dipentene, Ocimene and Licareol have been identified in bael and also some of these compounds have been shown to have antifungal and antibacterial activities. The most widely investigated compounds from *A. marmelos* were determined by reviewing and evaluating the items from the obtained bibliographic data [21, 22].

2.1.6 Pharmacological properties of Bael (Aegle marmelos)

Therapeutic benefits in the digestive system:

Bael is rich in phytoconstituents such as alkaloids, flavonoids, tannins and also essential oils which shows the gastro-protective effects. Research indicates that Bael possesses antidiarrheal properties due to its high tannin content which helps in the reducing intestinal inflammation and ultimately controlling fluid loss. Additionally Clinical studies have shown that Bael pulp can effectively manage the acute and chronic diarrhoea by modulating the gut motility and improving the stool consistency. Additionally, Bael contributing the role in alleviating constipation is notable because the fiber-rich content improves bowel movements and improves overall digestive health. Bael's laxative effect, attributed to its mucilage content which helps in the softening stools and preventing constipation.

Bael shows significant potential in the management of the peptic ulcers. Its flavonoids and phenolic compounds have demonstrated ulcer-healing properties by the promoting mucosal integrity and reducing gastric acid secretion. Overall, Complex therapeutic properties of bael make it a valuable natural remedy for gastrointestinal health [23].

Antioxidant property: The monosaccharide composition shows a major role in the antioxidant mechanism of polysaccharides. Bael fruit extract is rich in rhamnose and arabinose which act as the prevention of oxidative damage to lipids [24].

Anti-inflammatory Activity: Using a rat paw oedema model the A. marmelos was shown to have anti-inflammatory properties. The anti-inflammatory properties of the different bael leaf extracts were evaluated. In isolated guinea pig ileum and tracheal chain where the alcoholic extract of bael leaves shown a good relaxant effect and it responded histamine-induced contractions

which indicating that this extract may be responsible for these effects via inhibiting H1 receptor activity [16].

Antidiabetic Activity: Research has shown that bael fruit juice is more effective than the antidiabetic medication glibenclamide when consumed at 250 mg/kg. Bael fruit contains l-arabinose sugar which has selective inhibitory effects on the sucrose activity in the intestine. This results in the suppression of increased blood glucose levels after the sucrose ingestion. Moreover, l- arabinose helps in the regulation of blood glucose levels which leads to a reduction in obesity [25].

Cardiovascular Activity: Bael shows the impact on the blood pressure regulation is another important benefit. Studies have demonstrated that bael can helps in lower systolic and diastolic blood pressure. Potentially because of its vasodilatory effects and the presence of compounds which improves the endothelial function. Enhanced endothelial function contributes to better blood flow and reduced hypertension [23].

2.2 ECLIPTA ALBA (Bringraj)



FIGURE: ECLIPTA ALBA (Bringraj)

2.2.1 Taxonomical Classification of ECLIPTA ALBA[26]

Kingdom	Plantae
Subkingdom	Viridaplantae
Infrakingdom	Streptophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Infradivision	Angiospermae
Class	Magnoliopsida
Superorder	Asteranae
Order	Asterales
Family	Asteraceae
Genus	Eclipta
Species	Alba
Common name	False Lily, Bhringraj

2.2.2 Vernacular names of ECLIPTA ALBA (Bringraj)[27,28]

Languages	Names
English	Trailing Eclipta
Sanskrit	Keshraj, Tekraja, Bhrunga, Markava, Bhangara
Hindi	Bhangara, Bhangaraiya, Mochkand, Babri
Gujarati	Bhangaro, Bhangro, Kalugranthi, Dodhak, Kalobhangro
Bengali	Bheemraja, Kesuriya, Kesari, Kesuri, Kesuti
Marathi	Bhangara, Bhringiraja, Maka
Kannada	Garujalu, Gurugada, Soppu, Keshavardhana, Kodigaraju
Malayalam	Kayyonni, Knnunni
Tamil	Karisalankanni, Karisalanganni, Karisalai, kaikeshi
Telugu	Guntakalagara, Guntagalagara
Arab	Kadim-el-bint
Assam	Bhringraja
Oriya	Kesara, Kasarda
Santhal	Lal Kesari
Sindh	Tik
Punjabi	Bhangra
Urdu	Bhangra

2.2.3 Botanical Description[29]

Eclipta alba is an annual herb growing up to 30-40cm tall and erect or sometimes rooting occurs at the nodes.

Leaves: The leaves are sessile to sub-sessile. It is opposite 1.2 to 2.3 cm wide and 2.2 to 8.5 cm long oblong, lanceolate and strigose with fine hairs on both sides of the surface of leaves.



Flowers: The flowers are white, small and arranged in the form of tiny bundle. The leaf axis gives rise to the flowering stem. The inflorescence is racemose and the bloom can be actinomorphic, zygomorphic, pentamerous or unisexual. Androecium with five stamens an epipetalous filament, a free anther and an obtuse base, gynoecium with two carpels which fused to formed the fruit, Ovary inferior and unilocular with one basal ovule.

Fruit: Fruit of bringraj is the achenes cuneate, pappus and one seeded with slight wing and the brown in appearance.

Roots: Roots are cylindrical in shape and grey in colour.

Seeds: Seeds are dark brown and hairy outer layer which 0.2 to 0.25cm in height and width is 0.1cm and also non-endospermic dicotyledon.

2.2.4 Geographical Description

E. alba is found as a wild plant in tropical and subtropical regions of the world such as South America, Asia and Africa at height of up to 2000 m. *E. alba* is found throughout world in which some countries like India, China, Thailand, Brazil, Taiwan, Indonesia, Japan, the Philippines, Bangladesh, and United States. In India bringraj is mainly found in states like Assam, Bihar, Uttar Pradesh and Manipur [30].

2.2.5 Phytochemical Constituents of bringraj[31]

A wide range of primary and secondary metabolites have been extracted from the plant *Eclipta alba* which contains phytochemicals such as alkaloids, alkenynes, cardiac glycosides, steroids, triterpenes, phytosterol, flavonoids, coumestans, glycosides, triterpinoids and saponins. Among these, flavonoids, triterpenes, coumestans and also steroids are considered the

key primary phytoconstituents. Different parts of the plant are contains different constituents.

Coumestan: Coumestan is derivative of secondary metabolites phytoestrogen which is normally found in the vascular plants. Its makes the central core of different compounds which are collectively known as coumestans. Phytochemical investigation of *Eclipta alba* in different previous study exposed the plant contains a large amount of coumestans. The major coumestan extracted from the *Eclipta alba* species includes wedelolactone (0.5-0.55%) and demethylwedelolactone and demethylwedelolactone-7-glucoside which is present in the leaves of *Eclipta alba* which shows the Anticancer, trypsin inhibitor, antivenom, dye(cosmetic) and antihepatotoxic activity.

Alkaloids: The major alkaloids found in the *Eclipta alba* is [(20S) (25S)-22,26-imino-cholesta-5,22(N)-dien-3 β -ol] known as verazine. The other alkaloids found in this plant are [20-epi-3-dehydroxy-3-oxo-5,6-dihydro-4,5-dehydroverazine], [(20R)-20-pyridyl-cholesta-5-ene-3 β ,23-diol] (ecliptalbine), [(20R)-4 β -hydroxyverazine], [4 β -hydroxyverazine], [(20R)-25 β -hydroxyverazine] and [25 β -hydroxyverazine]. Beside these, other types of steroids including stigmasterol, daucosterol and β -sitosterol aslo have been extracted from the *Eclipta alba* which shows the Lipid lowering and Analgesic activity.

Flavonoids: More than 10 flavonoids have been isolated from *Eclipta alba*'s aerial parts in the forms of flavonoids, flavones and isoflavones. *Eclipta alba* contains several types of flavones including their glycosides these are luteolin, apigenin, diosmetin, apigenin-7-o-glucoside, buddleoside and luteolin-7-o-glucoside. Isolated isoflavones in previous several studies are paratensein, orobol and their subtypes 7-O-methylorobol-4'-O- β -D-glucopyranoside, Pratensein-7-O- β -D-glucopyranoside and 3'-O-methylorobol which have been found in the aerial

part of the *Eclipta alba* which shows the Anticancer, antioxidant, Anti allergic and Anti-inflammatory activity and also recognized in the medicinal community for anti-HCV, osteoprotective, anti-inflammatory and anti-HIV effects.

Triterpenoids: *Eclipta alba* is rich in triterpenoids contains a large group of organic compounds which present in the plant primarily as glucosides called triterpenoid saponins. To date, around 37 different triterpenoids have been isolated from *E. alba*. The main triterpenoids identified include eclalbasaponins I–XIII, ecliptasaponins A–D, oleanolic acid, echinocystic acid, β -amyrin, ursolic acid, α -amyrin, and their derivatives. Especially, ecliptasaponin C and D are new triterpenoid glucosides which are recently identified in the whole plant. In addition, α -amyrin, β -amyrin, ursolic acid, oleanolic acid and wedelic acid are among the more recently isolated triterpenoids from this species. Some triterpenoids show different biological activities including cytotoxic, hypoglycemic, anti-fibrotic and anti-osteoporotic effects.

2.2.6 Pharmacological properties of Bringraj (*Eclipta alba*)

Immunomodulatory Activity: Bringraj was found that coumestans such as Wedelolactone had shown inhibitory action against trypsin which supports its used as an immunomodulatory. The Wedelolactone is obtained from the methanol extract of the whole plant of *Eclipta* species was reported to shown immunomodulatory responses in mice at different dose range from 100 to 500 mg/kg. Various parameters such as carbon clearance, antibody titer and cyclophosphamide immunosuppression were accessed which showed the significant rise in the phagocytic index and the antibody titer which resulted in a

significant ratio of the phagocytic index and white blood cells(WBC) count [30].

Anti-ulcer and Anti-colon Cancer Activity: The ethanolic extract showed potent anti-ulcer effects in a dose-dependent manner. Significantly decreasing ulcerative lesions and reducing lipid peroxidation in a rat model. Similarly, The methanol extracts from *Eclipta* species significantly decreased the formation of gastric ulcers and lowered inflammation in mice with aspirin-induced ulcers. Additionally, In MTT assays, crude methanol extracts of *Eclipta* species exhibited targeted anti-cancer activity against the HCT-116 colon cancer cell line. These results suggest that the *Eclipta* species contains bioactive compounds with potential applications in colon cancer treatment [32].

Skin Diseases: A formulation containing powdered of *Eclipta alba* has demonstrated efficacy in the treating skin conditions which achieving complete remission in 22.6% of patients diagnosed with “Vicharchika” (eczema) and successfully preventing recurrence in 89.5% of affected individuals [27].

Antioxidant property: Oxidative stress causes the release of free radicals, contributing to various disorders including neurodegenerative diseases, cancer, atherosclerosis and also angina pectoris. Anti-oxidants because of their scavenging activity which are useful for the management of these diseases. *Eclipta alba* is a rich natural source of antioxidants such as phenolic acids, flavonoids and terpenoids which effectively counteract oxidative stress. Phenolic compounds act as reducing agents, singlet oxygen quenchers, hydrogen donors and metal chelators. Treatment with *Eclipta alba* significantly lowers TBARS, hydrogen peroxide and also nitric oxide levels while restoring antioxidant defences [33].

Neuropharmacological activities: Aqueous and hydro-alcoholic extracts of the *Eclipta alba* investigated for their neuropharmacological

activity which including sedative, muscle relaxant, anxiolytic, nootropic and also anti-stress properties. These properties were evaluated by oral doses of 150 mg/kg and 300 mg/kg. After that the results shown the potential of these extracts to control central nervous system functions relevant to relaxation, anxiety reduction, cognitive enhancement and also stress reduction [32].

Cardiovascular effects: Ethanol extract from *Eclipta alba* leaves and also leaf capsules was tested for the heart inhibitory activity in the isolated frog hearts. The extracts showed negative inotropic and negative chronotropic effects as well as reduced in the cardiac output. Callus extract showed a higher inhibitory effect on the heart than the leaf extract at doses of 20 mg [32].

Other Medicinal Uses: Alopecia (promotes hair growth), Varnya (skin disease controller), Reduce Constipation, As Carminative, Digestive stimulant, Diarrhoea and Dysentery, Hepatic, Anthelmintic, Anti-asthmatic, Anti-epileptic, Anti-aging, Anti-headache, Anti-diabetic, Anti-diuretic, Anti-fever, Anti-acne, Anti-microbial, Anti-piles, Analgesic and Anti-inflammatory, Immunostimulatory, Improve the strength of teeth, Muscle relaxant, Osteoblast differentiation (Bone Cell formation), Check alzheimer's disease, Hepatic steatosis, Control folliculitis, Regulate hypertension, Manage scalp psoriasis (Itchiness) [34].

2.3 Convolvulus pluricaulis (Shankhpushpi)



FIGURE: Convolvulus pluricaulis (Shankhpushpi)

2.3.1 Taxonomical Classification of Convolvulus pluricaulis[35]

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Super-division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Sub-class	Asteridae
Order	Solanales
Family	Convolvulaceae
Genus	Convolvulus
Species	pluricaulis

2.3.2 Vernacular names of Convolvulus pluricaulis [36]

Languages	Names
Sanskrit	Sankhapuspi
Hindi	Shankhpushpi, Aparajit
English	English speedwheel
Tamil	Sanghupushpam, kakkurattai, Kakattam, Kakkanangudi, Karakhuratt
Telugu	Shankhapushpi
Panjabi	Shankhpushpi, Sankhapuspi, Sankhahuli
Bengali	Sankhapuspi
Gujarati	Shankhahali
Urdu	Sankhali
Kannada	Bilikanthisoppu, Shankhapushpi, Shankhauli
Malayalam	Krsna kranti, Vishnukranthi
Marathi	Shankhavela, Sankhahuli, Sankhapuspi
Oriya	Krishna-enkranti, Sankhapuspi
Tibetan	Shankhpushpi

2.3.3 Botanical Description[37]

Convolvulus pluricaulis is a perennial plant with branches which spread widely along the ground and reaching lengths of up to 30 cm.

Flowers: The flowers are either white or purple in colour which growing singly or in pairs along with sessile or sub-sessile in the leaf axils.

Fruits: The fruits are oblong-globose capsules with a coriaceous and pale brown pericarp.

Leaves: The leaves are short-petioled, linear-lanceolate and acute in shape. Also leaves are hairy on both sides which is about 1-2 cm in length and 0.1-0.5 cm in width along with a light green colour.

Stem: The stems are cylindrical with hairy nodes and internodes in structure.

Roots: Its roots are usually branched, cylindrical and ribbed with some rough nodules along the stem. The smaller roots range from 1-5 cm in the length and 0.1-0.4 cm in thickness with a colour which transitions from brown to light brown.

Seeds: The seeds are brown and minutely puberulous.

2.3.4 Geographical Description

Convolvulus pluricaulis Known as Aloe weed in English, the herb is commonly found in India [38,39]. It can be found in the plains of Chota Nagpur, Punjab, Uttar Pradesh, Haryana, Rajasthan, and Bihar in India [40].

The present study was conducted in Barmer, Chohtan and Baitu Tehsil of Barmer district of Western Rajasthan. Barmer district was purposively selected for the present investigation because it is one of the larger Medicinal crop district under the dryland condition in Western region of the Rajasthan. Three talukas were selected based on the maximum area under medicinal crop. In which From Chohtan Tehsil - 17 villages 52 respondents and from Barmer Tehsil - 5 villages 9 respondents were selected who were growing Shankhpashpi. As a result, respondents growing Shankhpashpi [41].

2.3.5 Phytochemical Constituents of *Convolvulus pluricaulis*

Convolvulus prostratus (CP) have been recognised to various phytoconstituents which belonging to

the chemical family of alkaloids, flavonoids, coumarins and polyphenols. Among these phytoconstituents, certain compounds are known to be present at a higher concentration (almost 20% w/w) and are known as major phytoconstituents.

Alkaloids: The plant contains several alkaloids such as convolamine, convoline, convolvine, convosine, evolvine, phyllabine, subhirsine and sankhpuspine. These compounds shows the antihypoxic anti-inflammatory, antiepileptic and nootropic activity[42,43].

Flavonoids: Major flavonoids in *convolvulus prostratus* are kaempferol and quercetin. Kaempferol shows strong antioxidant, anti-inflammatory and anti cancer activity. It also play role in the regulation of lipid metabolism and bone resorption [44,45].

Coumarins and Coumarin Glycosides: The key coumarins in *convolvulus* are ayapanin, scopoletin and scopolin. Scopoletin shows antifungal, anti-allergic and also anti-aging properties[46,47]. Ayapanin play role in the improves spatial memory [48].

Phenolic and Carboxylic Acids: Hydroxycinnamic acid and other phenolics present in the plant which act as strong antioxidants, scavenging free radicals and also protecting neurons from the oxidative stress [49].

Triterpenoids and Sterols: The Compounds like taraxerol, taraxerone and β -sitosterol are present in *Convolvulus prostratus*. In which Taraxerol exhibits anti-inflammatory and anticancer potential. β -sitosterol shows anti-proliferative, anti-pyretic and pro-apoptotic effects contributing to overall neuroprotective and cardioprotective action [50].

2.3.6 Pharmacological properties of *Convolvulus pluricaulis*

Antioxidant effect: The study done on aqueous extract *Convolvulus pluricaulis* showed



significant antioxidant effect by scavenging the free radicals of stressed induced conditions that may be due to the presence of flavonoids, alkaloids and glycosides [51].

Anti-inflammatory and antipyretic effect: The ethanolic extract of *Convolvulus pluricaulis* showed the markable result as antipyretic and moderately anti-inflammatory effect [52].

Neuroprotective effect: The neuroprotective study done on aluminium induced toxicity in brain of rats in which aqueous extract of *Convolvulus pluricaulis* administered for 3 months to the rats. It indicated the prevention of the neurotoxicity and reduced the oxidative stress. It showed the positive effect in altered activity of proteins on various level of cholinergic synapse.

Anti gastric & Antiulcer effect: The *Convolvulus pluricaulis* in the form of the fresh juice was given for 5 days so it can reported the significant result in protecting the gastric mucosa by the production of mucin.

Effect of CNS: The study was done on the three varieties of *Shankhpushpi* showed different results. From this, it is concluded that all three plants are possess memory-enhancing, anxiolytic and CNS-depressant activity with *Convolvulus pluricaulis* showing the maximum activity. The reported results of memory enhancing activity advise that *Convolvulus pluricaulis* should be used as the true source of *Shankhpushpi* [53].

3 HERB HERB INTERACTIONS

Pharmacokinetic synergism:

This involves one herb facilitating the absorption, distribution, metabolism or elimination (ADME) of another. *Bael* contains significant amounts of tannins and saponins [54]. The high antibacterial activity in the methanolic extract may be due to the presence of tannins, flavonoids and Saponins are surface-active agents that may increase the permeability [55]. Further, 'Metabolism' certain

components in one herb may inhibit liver enzymes (like Cytochrome P450) responsible for breaking down the active constituents of another thereby extending their half-life and therapeutic duration [56].

Pharmacodynamic synergism:

This occurs when multiple herbs with similar therapeutic effects act via different molecular pathways to produce a superior outcome [56].

Bael exhibits acetylcholinesterase (AChE) inhibition which preventing the breakdown of acetylcholine in the synaptic cleft and offers radioprotective benefits to neurons [57].

Bhringraj supports the neuroprotection and neutralizing oxidative stress through its high antioxidant capacity and also potentially modulating the neurotrophic factors [58].

Shankhpushpi provides direct GABAergic stimulation and blocks the muscarinic receptors to enhance memory and reduce anxiety [59].

Antidiabetic:

The combination also shows potent synergistic potential in metabolic regulation. Both *Bael* and *Bhringraj* have significant antidiabetic properties with studies showing that *Bael* can regenerate pancreatic beta-cells and upregulate GLUT4 expression for better glucose uptake [60]. *Bhringraj's* antihyperglycemic activity is comparable to the allopathic drug *Metformin* [61]. When these are combined the antidiabetic effect is more markedly observed than in individual treatments, reduction in blood glucose and show the hypoglycemic activities of both extract by orally [62]. The alcoholic extract of *Shankh pushpi* used for the treatment of hyperglycemia (In vitro) and which are effectively produced the Antidiabetic effect in the human body [63].

Antihypertensives:

Shankhpushpi's natural hypotensive (blood pressure lowering) properties may cause an additive effect when combined with prescription antihypertensives (like beta-blockers or calcium

channel blockers) medications which leading to dizziness or fainting from the excessively low blood pressure [63].

CONCLUSION

Celiac disease remains a complex and systemic immune-mediated condition that presents significant diagnostic and management challenges. While a strict & lifelong gluten-free diet is currently the only recognized standard of care. It often fails to completely alleviate symptoms or restore full quality of life for all patients. This review highlights that we need to find new and also additional treatments for the celiac disease because the current medical options are not yet enough to fully manage it.

The investigation of medicinal plants like *Aegle marmelos* (Bael), *Eclipta alba* (Bringraj) and *Convolvulus pluricaulis* (Shankhpushpi) because they have full of healthy natural compounds such as flavonoids, alkaloids and tannins. These phytochemicals are provide essential pharmacological benefits such as anti diarrheal, anti-inflammatory, antioxidant and also gastro-protective activities which directly address the underlying oxidative stress and intestinal inflammation characteristic of the disease.

The combination of Bael, Bhringraj and Shankhpushpi in oral formulation offers a potent synergistic blend of neuroprotective, hepatoprotective and metabolic regulating agents. This "Medhya" trio utilizes complementary molecular mechanisms to enhance cognitive function, manage stress and stabilize the metabolic markers. When consumed as an orally, the preparation is generally may be safe and provided the consumer is aware of potential interactions with prescription medications such as sedatives, anticoagulants and antidiabetics and also not consume in higher amount.

In summary, integrating botanical interventions alongside traditional dietary management offers a

potential pathway to improved patient comfort and better systemic symptom control of the Celiac disease.

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