# Formulation & Evaluation of Polyherbal solution for Prognosis of IgA Vasculitis

Sumit Devkar\*<sup>1</sup>, Piyush Jangam<sup>2</sup>, Yogesh Bafana<sup>3</sup>, Pratik Jadhav<sup>4</sup>, Sagar Jadhav<sup>5</sup>, Aarti Shete<sup>6</sup>, Naziya

Pathan<sup>7</sup>

Student<sup>1,4,5,6,7</sup>, Associate Professor<sup>2</sup>, Principal<sup>3</sup>

Department of Pharmacology, Arihant College of Pharmacy, Ahmednagar, Maharashtra, India, 414005

Abstract: IgA Vasculitis is a systemic inflammation of small vessels.it is an autoimmune disorder in which IgA antibodies abnormally attacks hosts bodily cells, particularly to the blood vessels cell. IgAV is the most common form of vasculitis in children. IgA vasculitis spontaneously resolves in 94% of children and 89% of adults, and that's why making supportive treatment is the primary management strategy. Present study aimed to develop polyherbal formulation for prognosis in IgA vasculitis. In this study, Herbal solution was formulated containing suitable ingredient such as Asparagus racemosus, Zingiber officinale, Borago officinalis, Withania somnifera in different proportions to formulate and evaluate its physicochemical properties. Systematic reviews have shown that steroids do not prevent complications and should not be used prophylactically. Herbal drugs used in formulation acts by different mechanisms which aims to betterment of life quality diseased patient.

*Keywords*: IgA, Vasculitis, Purpura, HSP, Henoch-Schönlein purpura.

# I.INTRODUCTION

The human body is surrounded by the external environment. The skin is the outermost organ of the human body which is exposed to various environmental factors. Cutaneous immune response acts here to protect the host human body This selfdefense action against the external environment sometimes triggers excessive inflammatory reactions, namely autoimmune reactions. (1). Immunoglobulin A is a member of the human immunoglobulin family(4).It is an essential immune component that drives the host immune response to the external environment(1).IgA vasculitis formerly known as Henoch-Schönlein purpura, represents the nongranulomatous systemic vasculitis(2). Henoch-Schönlein purpura (HSP) is a systemic vasculitis caused by acute perivascular deposits of IgA and complement 3 (C3) in small blood vessels (3). It is characterized by inflammation of the blood vessels, which can restrict blood flow and damage vital organs and tissues. HSP is mostly seen in small childrens.

# **II.EPIDEMIOLOGY**

90% of cases occur under the age of 10 years. Therefore seen regularly by pediatricians. In children, it has a slight male predominance (1.5:1 male: female ratio). and adults have higher frequency of joint involvement when compared to children. IgAV can occur in any race and it predominates in certain parts of the world such as Korea and Japan(17).

#### **III.DIAGNOSIS**

IgA vasculitis should be suspected in patients presenting with palpable purpura who also develop arthralgias (75% of patients) and abdominal pain (50% to 65% of patients) (8).

Useful studies include a complete blood count to exclude blood loss and determine the platelet count; a coagulation profile to exclude coagulopathy; electrolytes and renal function tests to exclude renal disease; and a serum albumin test to assess for intestinal protein loss (12). Skin biopsy is needed only in cases where the diagnosis is unclear The fecal calprotectin level may be a reliable marker for gastrointestinal involvement (13). A renal biopsy should be performed if an IgA vasculitis patient has severe proteinuria (>250 mg/mmol for at least 4 weeks (14). More recently modified semi-quantitative classification (SQC) scores have been proposed to enhance the sensitivity in predicting the renal outcome in IgAV(15).

Because IgAV can affect all organ systems, a full physical examination is indicated.

# **IV.SYMPTOMS**

Signs and symptoms may develop over days to weeks in any sequence(9).

• *Rashes*: It begins with erythematous, macular, or urticarial lesions and progresses to blanching papules and later to palpable purpura. Rashes are seen in about 95-100% of cases. Rashes are seen on back and buttocks, ankles and lower legs, face, trunk, and upper extremities. Rash may be itchy but is rarely painful.



Figure 1: Progression of rash in immunoglobulin A vasculitis -Early stage



Figure 2 :purpura develop over few days.



Figure 3 : Petechiae and purpura at different stages of development

- *Arthritis*: Joint pain and abdominal pain are seen in 50-75% of children. whereas adults are more likely to have lower-extremity edema and hypertension (10). joints of the lower limb. Joints of the feet and ankles being most commonly involved in arthritis followed by knees, wrists, elbows, and hands (12).
- *GI problems*: Emesis and gastrointestinal bleeding can occur in approximately one-third of patients (5). Acute involvement of the GI tract impacts the short-term prognosis of the disease. Emesis and gastrointestinal bleeding can occur in approximately one-third of patients. 30% of patients experience gastrointestinal bleeding (5). Acute involvement of the GI tract impacts the short-term prognosis of the disease. It can extend to include acute GI bleeding. GI bleeding has been linked to the need for a longer hospital admission (16). and in severe cases it warrants acute immunosuppressive treatment

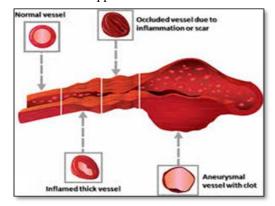


Figure 4: gastrointestinal damage

• *Kidney inflammation*: long-term prognosis depends on the severity of the kidney disease. IgA vasculitis in adult patients showed a high prevalence of IgA nephritis. Renal disease typically develops within one to three months after the rash, but it may be delayed up to six months (11).

# V.PHYSIOLOGY

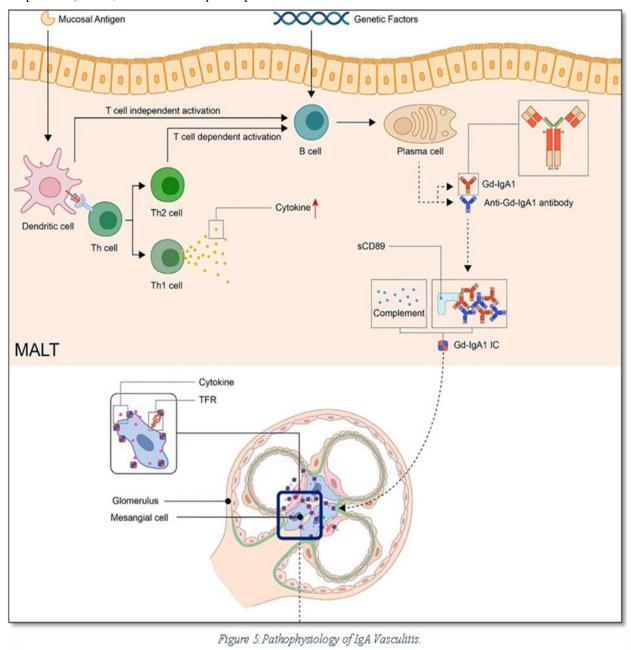
Immunoglobulin A (IgA) is the most abundant type of antibody in the body. Physiologically it serves to protect the mucosal tissues from microbial invasion and maintain immune homeostasis. Secretory IgA (SIgA) neutralise or block the activity of a range of viruses, bacteria, and protozoa, and prevent their attachment to host cells.

# VI.PATHOPHYSIOLOGY

The mucosal antigen is encountered by dendritic cells. Dendritic cells represent this antigen to Thelper cell. Thelper cells activate B-cells in MALT through T-cell-dependent or independent ways. With genetic factors, the activated B-cells become plasma cells and produce Gd-IgA1. Gd-IgA1 and anti-Gd-IgA1 autoantibodies form circulating immune complexes together with other components (including sCD89 or complements). Then, the immunocomplex deposit at

organs and activate inflammatory responses. In the kidney, the immunocomplex can activate mesangial cells through TfR, leading to the apoptosis of renal cells and recruitment of inflammatory cells.

Symptoms of IgA vasculitis typically last one to two months, and most patients recover on their own without treatment. Therefore, treatment is usually aimed at relieving minor symptoms until they dissipate. For that purpose we have developed a polyherbal solution.



# VII. MATERIAL AND METHODOLOGY

<u>Collection of Crude drugs:</u> Taxonomically identified and authenticated roots of Asparagus racemosus (Liliaceae) commonly known as Shatavari(6), Rhizomes of Zingiber officinale root (Zingiberaceae), fresh leaves of Borago officinalis (Boraginaceae) and Roots of Withania somnifera (Solanaceae) known commonly as ashwagandha were purchased from local herbal drug store.

These Crude drugs (Except Borago leaves) were subjected to shed drying. After sufficient drying they were powdered with help of various milling techniques. Ensured the proper milling of each Crude drug.

## • Asparagus racemosus

Synonym: Satawar, Satamuli, Satavari

<u>Biological source</u>: It is obtained from dried Roots of plant Asparagus racemosus belonging to family Asparagaceae

<u>Uses</u>: it is used as immunemodulatory (immunosuppresants) agent.



Figure 6: Asparagus racemosus

# • Zingiber officinale

# Synonym : Ginger

<u>Biological source</u>: It is obtained from dried rhizomes (underground stem) of plant Zingiber officinale belonging to family Zingiberaceae

uses: it is used as Anti-inflammatory agent.



Figure 7:Zingiber officinale

• Borago officinalis

Synonym: starflower, ajwain

<u>Biological source</u>: It is obtained from fresh leaves of Borago officinalis belonging to family\_Boraginaceae <u>uses</u>: it is used as Anti-inflammatory agent.

• *Withania somnifera* <u>Synonym</u>: ashwagandha, winter cherry





<u>Biological source</u>: It is obtained from dried Roots of Withania somnifera belonging to family Solanaceae <u>Uses</u>: it is used as Antioxidant, immunosuppressant agent.



Figure 1: Withania somnifera

Drug	Use	
Asparagus racemosus	Immunomodulatory	
Zingiber officinale	Anti-inflammatory	
Borago officinalis	Anti-inflammatory	
Withania somnifera	Antioxidant,	
	immunosuppresant	
Water	Vehicle	

Table 1: Useful pharmacological properties of Herbaldrugs.

<u>Preparation of decoction</u> :5gm of each powdered ingredient was mixed in 200 ml water in Beaker separately.Fresh leaves of borago was taken in beaker along with 200 ml Water. Then they were subjected to heating mantle for boiling. Heating was discontinued once total volume became one forth part of initial volume. The decoction preparation was then filtered through a muslin cloth followed by filtration with filter paper and kept at 4°C until its use.

<u>*Preparation of polyherbal solution*</u>: Finally polyherbal solution was formulated by mixing individual decoctions as per formula table.

Table 2:Formula table

Drug	Quantity		
	F1	F2	F3
Asparagus racemosus	4	5	2
Zingiber officinale	3	2	3
Borago officinalis	6	3	1
Withania somnifera	2	3	4
Water	5	7	10

#### VIII. EVALUATION OF FORMULATION:

1. Colour examination -

1) 5ml of prepared Solution was taken on a watch glass.

2) Watch glass placed against white background in white tube light.

3) Colour was observed by naked eyes.

2. Odour examination -

1) 2ml of prepared solution was taken and smelled individually.

2) The time interval between 2 smelling was 2 minutes to nullify effect of previous smelling.

3. Taste examination -

A pinch of final solution was taken and examined taste buds of tounge.

# 4. Transparency Examination-

1) Take 5ml Herbal solution in Test Tube.

2) Observe herbal solution against Bright white background for colour.

# 5. pH Determination-

1) 10 ml of prepared solution taken in 100 ml of volumetric flask.

2) Make up the volume to 100 ml with distilled water3) Sonicate for 10 Min.

4) pH was measured by using digital pH meter.

## 6. Viscosity Determination-

1) Placed the viscometer in vertical position on a suitable stand.

2) Filled water in dry viscometer up to mark G.

3) The time was counted in second for water to flow from mark A to mark B.

4) This step was repeated at least 3 times to avoid error.

# IX. RESULT

The Herbal formulation was prepared successfully by admixing the predetermined amount of the aqueous extracts of all the ingredients. Evaluation of polyherbal solution was carried out and result of evaluation study was as follows:

Table 3: Result of Evaluation tests.

Evaluation	F1	F2	F3
Test			
Colour	Greenish	Yellowis	Yellowis
Examination	Yellow	h-Brown	h-Brown
Odour	Aromatic	Aromatic	Aromatic
Examination			
Taste	Slightly	Slightly	Slightly
Examination	Bitter	Bitter	Bitter
Transparen	Transpar	Transpar	Transpar
cy	ent	ent	ent
Examinati			
on			
pН	6.2	6.0	6.3
Determinati			
on			
Viscosity	0.01323	0.01150	0.01294
Determinati			
on			

# X. CONCLUSION

The present study was carried out with the aim of preparing the polyherbal solution for prognosis of IgA Vasculitis which will provide symptomatic relief from IgA vasculitis. Herbal solution was formulated using aqeous extracts of various herbal drugs. Present study involves use of Asparagus racemosus, Zingiber officinale, Borago officinalis, Withania somnifera instead of synthetic drugs. To evaluate for good product performance of the prepared herbal solution, many tests were performed. The results of the evaluation study of the developed herbal solution revealed a comparable result for quality control test, but further scientific validation is needed for its overall quality

IgA vasculitis is common type of child Vasculitis About one-third of individuals who have IgA vasculitis will experience a relapse. Several studies have evaluated the anti-inflammatory action and therapeutic potential of omega-3 fatty acids in IgA and nephritis(1). Recent vasculitis drug developments and the presence of COVID-19 have revealed that bacterial and viral agents can also trigger IgA vasculitis(1). Effective treatment of IgA vasculitis may require the coordinated efforts and ongoing care of a team of medical providers and specialists. The present study help to develop affective and safe polyherbal solution for enhancing patient life quality. Furthermore, the role of IgA in the development of vasculitis needs to be further explored. An in-depth understanding of how acquired and innate immunity participates in the pathogenesis of IgAV may provide the possibility of targeted treatments.

# XI. ABBREVIATION

IgA	–Immunoglobulin A.
HSP	-Henoch–Schönlein purpura.
IgAV	-Immunoglobulin A Vasculitis.
COVID-19	-Corona VIrus Disease of 2019.
рН	- Potential of Hydrogen.
GI	-Gastro Intestine.
SQC	-Semi Quantitative Assay.
ADCC	-Antibody-Dependent Cell Cytotoxicity.
CDC	-Complement-Dependent Cytotoxicity.
Gd-IgA1	-Galactose-deficient IgA1.
MAC	-Membrane Attack Complex.
MALT	-Mucosa-Associated Lymphoid Tissue.
NET	-Neutrophil Extracellular Traps.
TfR	-Transferrin Receptor.
SIgA	- Secretory IgA.

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#### XIII. CONFLICT OF INTEREST

Authors declare no conflict of interest.

#### XIV. REFERENCE

- Sugino H, Sawada Y, Nakamura M. IgA Vasculitis: Etiology, Treatment, Biomarkers and Epigenetic Changes. Int J Mol Sci. 2021 Jul 14;22(14):7538. doi: 10.3390/ijms22147538. PMID: 34299162; PMCID: PMC8307949.
- Ozen S, Pistorio A, Iusan SM, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. part II: final classification criteria. Ann Rheum Dis. 2010;69(5):798–806.

doi:10.1136/ard.2009.116657

- Rai A, Nast C, Adler S (December 1999). "Henoch-Schönlein purpura nephritis". Journal of the American Society of Nephrology. 10 (12): 2637–44. doi:10.1681/ASN.V10122637. PMID 10589705
- 4) Marieke H. Heineke, Aranka V. Ballering, Agnès Jamin, Sanae Ben Mkaddem, Renato C. Monteiro, Marjolein Van Egmond, New insights in the pathogenesis of immunoglobulin A vasculitis (Henoch-Schönlein purpura), Autoimmunity Reviews, Volume 16, Issue 12, 2017, Pages 1246-1253, ISSN 1568-9972, https://doi.org/10.1016/j.autrev.2017.10.009.
- 5) Saulsbury F.T. Clinical update: Henoch-Schönlein purpura. *Lancet*. 2007;369:976–978.

doi: 10.1016/S0140-6736(07)60474-7. [PubMed] [CrossRef] [Google Scholar] [Ref list]

- Thatte U, Chhabria S, Karandikar SM, Dahanukar S. Immunotherapeutic modification of E. coli induced abdominal sepsis and mortality in mice by Indian medicinal plants. Indian Drugs. 1987;25:95–97. [Google Scholar] [Ref list]
- Kuttan G. Use of Withania somnifera Dunal as an adjuvant during radiation therapy. Indian J Exp Biol. 1996;34 (9):854-856.
- 8) Trapani S, Micheli A, Grisolia F, et al. Henoch Schonlein purpura in childhood: epidemiological and clinical analysis of 150 cases over a 5-year period and review of literature. Semin Arthritis Rheum. 2005;35(3): 143-153.
- Reamy BV, Williams PM, Lindsay TJ. Henoch-Schönlein purpura. Am Fam Physician. 2009;80(7):697-704. Accessed March 6, 2020. https://www.aafp.org/afp/2009/1001/p697.html
- 10) Lu S, Liu D, Xiao J, et al. Comparison between adults and children with Henoch-Schönlein purpura nephritis. *Pediatr Nephrol.* 2015;30(5):791-796.
- 11) Chen JY, Mao JH. Henoch-Schönlein purpura nephritis in children: incidence, pathogenesis, and management. World J Pediatr. 2015;11(1):29-34.
- 12) Jauhola O, Ronkainen J, Koskimies O, et al. Clinical course of extrarenal symptoms in Henoch-Schonlein purpura: a 6-month prospective study. Arch Dis Child. 2010;95(11):871-876.
- 13) Kanik A, Baran M, Ince FD, et al. Faecal calprotectin levels in children with Henoch-Schönlein purpura: is this a new marker for gastrointestinal involvement?. Eur J Gastroenterol Hepatol. 2015;27(3):254-258.
- 14) Wulffraat NM, Vastert B, consortium S. Time to share. Pediatr Rheumatol Online J. (2013) 11:5. doi: 10.1186/1546-0096-11-5
- Counahan R, Winterborn MH, White RH, Heaton JM, Meadow SR, Bluett NH, et al. Prognosis of Henoch-Schonlein nephritis in children. Br Med J. (1977) 2:11–4. doi: 10.1136/bmj.2.6078.1
- 16) Uehara E, Nagata C, Masuda H, Fujimori K, Kobayashi S, Kubota M, et al. Risk factors of long hospital stay for immunoglobulin a vasculitis: single-center study. Pediatr Int. (2018) 60:918– 22. doi: 10.1111/ped.13685

17) Huang X, Wu X, Le W, Hao Y, Wu J, Zeng C, et al. Renal prognosis and related risk factors for henoch-schonlein purpura nephritis: a chinese adult patient cohort. Sci Rep. (2018) 8:5585. doi: 10.1038/s41598-018-23638-2