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Ameliorating Effect of Stellaria Media, A Common Homoeopathic Medicine on Polyarticular Inflammatory Arthritis: Possible Role in Anti-Inflammatory Action

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ABSTRACT

Background: Polyarticular inflammatory arthritis (PIA), characterized by inflammation involving more than four joints, presents a significant clinical challenge due to pain, swelling, and progressive joint destruction. While conventional treatments offer symptomatic relief, the search for safer, cost-effective alternatives continues. Stellaria media, a plant-based Homoeopathic medicine, is traditionally known for its anti-inflammatory properties.

Objectives: This study aimed to evaluate the anti-inflammatory efficacy of hydro-ethanolic extract of Stellaria media through in-vitro assays and a clinical trial in patients with PIA.

Methods: The in-vitro component employed human peripheral blood mononuclear cells (hPBMCs) treated with lipopolysaccharide (LPS) to induce inflammation. These cells were exposed to varying concentrations of Stellaria media extract, and anti-inflammatory effects were assessed through MTT assay for cytotoxicity, ROS generation using H2DCFDA probe, and ELISA-based estimation of IL-6 and COX-2 levels. A one-month open-label, pre-test/post-test clinical study was concurrently conducted with 30 patients diagnosed with PIA. Participants received 0.5 ml of Stellaria media extract diluted in 15 ml distilled water, administered orally twice daily. Outcomes were evaluated using the Numerical Pain Rating Scale (NPRS), Erythrocyte Sedimentation Rate (ESR), and C-Reactive Protein (CRP).

Results: In-vitro analysis demonstrated that Stellaria media extract was non-cytotoxic and significantly reduced ROS levels, IL-6, and COX-2 expression in LPS-induced hPBMCs. Morphological preservation of cells was also noted in treated groups. Clinically, significant reductions were observed in mean ESR (22.8 to 16.5 mm/hr, $p < 0.05$), CRP (3.2 to 2.1 mg/dL, $p < 0.05$), and NPRS scores (7.13 to 3.27, $p < 0.0001$) after treatment.

Conclusion: The results from both in-vitro and clinical arms strongly suggest that Stellaria media possesses anti-inflammatory activity, possibly mediated through reduction of oxidative stress and downregulation of inflammatory mediators like IL-6 and COX-2. These findings support its potential as a cost-effective therapeutic option for managing polyarticular inflammatory arthritis. Further controlled trials with larger sample sizes and longer follow-up are warranted.

***(Keywords**: Stellaria media, Homoeopathy, Polyarticular arthritis, Anti-inflammatory, IL-6, COX-2)*

1. INTRODUCTION

Inflammation is defined as the local response of living tissue to injury from any agent. There are endogenous Inflammation is the local protective response of living tissue to injury from physical, chemical, or biological agents, mediated by a complex interplay of endogenous chemical mediators. These include cell-derived factors such as cytokines, interleukins, prostaglandins, leukotrienes, platelet-activating factors, and histamine, as well as plasma-derived mediators such as kallikrein, bradykinin, fibrinopeptides, plasmin, and complement proteins.[1]

Polyarticular inflammatory arthritis (PIA) is a type of inflammatory arthritis affecting more than four joints, with aetiologias that may be immune-mediated, infectious, crystal-induced, or idiopathic. It is characterized by mononuclear cell infiltration, tissue destruction, necrosis, and proliferative changes, leading to polyarticular pain, prominent morning stiffness, non-traumatic joint swelling, and sometimes fever. Laboratory findings may show elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels.[2] In India, PIA affects approximately 0.92% of adults, with an annual incidence of 20–40 new cases per 100,000 population, occurring more frequently in females. Managing PIA remains challenging, with the physician's role extending beyond symptom control to improving patients' quality of life.

Stellaria media (family Caryophyllaceae), an annual flowering plant, has a long history of traditional use for inflammatory conditions.[3] Hydro-ethanolic extracts prepared according to the Homoeopathic Pharmacopoeia of India contain secondary metabolites such as flavonoids, oligosaccharide stellariose, anthraquinone derivatives, fatty acids, steroidal saponins, and phenolic compounds, which have been associated with diverse pharmacological activities including anti-inflammatory, analgesic, antioxidant, antimicrobial, anti-obesity, antiproliferative, antidiabetic, and anxiolytic effects.[4] Preclinical research by Oyebamiji et al. demonstrated both anti-inflammatory and antioxidant potential of S. media, attributed to its rich phytochemical profile.[5] In animal models, methanolic leaf extract significantly reduced formalin-induced paw licking and albumen-induced paw oedema, with comparable effects to indomethacin.[6]

Additional studies have shown that S. media exhibits strong antioxidant activity through mechanisms such as ferrous ion chelation and radical scavenging (DPPH, ABTS assays), suggesting a role in protecting against oxidative damage.[7] A comparative phytochemical study from Pakistan confirmed that S. media, along with Trifolium repens and Pteridium aquilinum, is a rich source of antioxidant molecules.[8] Clinical investigations into homoeopathic approaches for arthritis, including randomized controlled trials, have reported significant improvements in pain, stiffness, grip strength, and articular index among patients receiving individualized homoeopathic medicines compared to placebo, without adverse effects.[9]

These findings collectively indicate that S. media may exert anti-inflammatory effects via both antioxidant mechanisms and downregulation of inflammatory mediators, supporting its potential as a cost-effective therapeutic option in PIA. The present study was therefore undertaken to evaluate the anti-inflammatory action of hydro-ethanolic extract of S. media using in-vitro assays on human peripheral blood mononuclear cells (hPBMCs) and clinical study in patients with polyarticular inflammatory arthritis

2. OBJECTIVES

- To understand the anti-inflammatory action of hydro -ethanolic extract of Stellaria media on RAW cell line: In vitro
- To study the role of hydro-ethanolic extract of Stellaria media in patients with polyarticular inflammatory arthritis and evaluate their role in anti-inflammatory action

3. METHODOLOGY:

4.1 In-vitro Study

Materials and Methods:

Chemicals

All the chemicals used were high quality analytical grade. Solvents were purchased from Merck, India. Lipopolysaccharide (LPS) and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), RPMI 1640 media and fetal bovine serum (FBS) were purchased from Sigma Aldrich (St. Louis, MO, USA). The ELISA kits were purchased from Cayman Chemicals, USA.

Preparation of Stellaria media

100mL of Stellaria media mother tincture (SM) was taken in a conical flask. The solvent from the SM was then removed by using rotary vacuum evaporator. Finally, the residues were collected and refrigerated at 4 °C until further analysis.

Invitro analysis: Cell culture treatments

Isolation of hPBMC

hPBMCs were isolated from heparinized venous blood via Ficoll density gradient centrifugation method. In brief, the blood sample was diluted with 2x volume of 1x PBS (pH 7.4) and carefully layered over an equal volume of Ficoll-paque in a 15 mL-conical tube. The suspension was centrifuged (400 xg, 30 min, 20 °C) and the upper layer was aspirated, leaving the mononuclear cell layer (lymphocytes, monocytes, and thrombocytes) undisturbed at the interphase. The mononuclear cell layer was transferred to a new conical tube, and 1x PBS was added. Following centrifugation (300 xg, 10 min, 20 °C), the supernatant was carefully removed. The cell pellets were resuspended with 1x PBS. Following centrifugation (200 xg, 10 min, 20 °C), the supernatant was carefully removed. The hPBMC pellets were obtained through centrifugation over Ficoll–Paque™ cushions of buffy-coat, and cell number was

counted using a cell counter. The cell suspension at density of 5×10^6 cells/mL was prepared in RPMI 1640 medium supplemented with 10% fetal bovine serum (RPMI-FBS) and incubated at 37 °C for 3 h. About 100µl of the suspension were cultured in 96-well plates and incubated with different concentrations of SM (6.25, 12.5, 25 and 50 µg/ml) for 24 h under identical environments.

Experimental design

hPBMCs Cells were divided into different groups.

- Group I was treated as normal control
- Group II was treated with 1µg/ml LPS
- Group III was treated with 1µg/ml LPS + Stellaria media (SM) (25 µg/ml)

It was maintained in the culture for indicated time. The supernatant of cultures was collected for the determination of inflammatory parameters and morphological analysis

Analytical procedures

Cytotoxicity assay

Cytotoxicity was assayed by the modified tetrazolium salt 3-(4-5- dimethylthiozol-2-yl) 2-5- diphenyl-tetrazolium bromide (MTT) assay. PBMCs cells were plated with various concentrations of SM in 96-well microtiter plates (Nunc, Roskillde, Denmark) and then cultured for 24 h at 37C a 5% CO2 incubator. At culture termination, 10 µL of the MTT solution was added into each well and then cultured for 4 h at 37^0C in a 5% CO2 incubator. Then 100 µL of solubilized solution was added into each well. The plate was allowed to stand overnight in the incubator after evaluation for complete solubilization of the purple formazan crystals and measurement of the optical density (OD) at 570 nm by a microplate reader.

Morphological analysis

The observation of morphological changes of hPBMC was performed using a phase- contrast inverted microscope. Briefly, cells were incubated for 24 hours at 25µg/ml concentration of SM in a 60 mm diameter tissue culture dishes. The medium was discarded, and cells were washed once with PBS. The changes in the morphology of cells were observed to determine the alterations in hPBMCs cells and the images of the cells were grabbed at 20x by using the phase- contrast inverted microscope (Labomed, USA).

Determination of intracellular ROS generation

To study the total ROS content inside the cells, we use the H_2DCFDA probe. The attached PBMCs in RPMI are treated with the SM for 90s and the intracellular ROS content is measured on day 2, 4 and 8 with and without the presence of 1 µM trolox (ROS scavenger), using 10 mM of H_2DCFDA to each sample, and kept at 30 °C incubation for 1 h. Subsequently, the cells are washed twice with PBS and the intracellular ROS generation were determined by Phase contrast microscopy.

Estimation of IL-6 and COX-2

The release of IL-6 and COX-2 were measured in the supernatants of PBMC cells treated with LPS in the absence or presence of SM using ELISA kit (Cayman chemicals, USA). ELISA plate was divided into 6 different types of wells, i.e., blank, total activity (TA), non-specific binding (NSB), maximum binding (B0), standards (S) and sample wells. 100µl ELISA buffer was added to NSB wells, 50 µl ELISA buffer was added to B0 wells. 50 µl of standard was added to the standard wells from lowest concentration to highest. 50 µl samples were added per well. 50 µl AChE tracers were added to each well except TA and blank wells. 50 µl Monoclonal Antibody was added to all wells except TA, NSB and blank wells. The ELISA plate was covered with plastic film and kept for incubation for 18 hours at 4°C. After incubation the wells were rinsed five times with Wash buffer. 200 µl Ellman's Reagent was added to each well. 5 µl of tracer was added to TA wells. The plate was covered with the plastic film and kept for incubation in dark for 60-90 minutes. Then, the plate was read at a wavelength between 405-420nm.

4.2 Clinical Study

Source of data:

Patients between 18 years to 60 years of age attended the outpatient department and peripheral clinics of Homoeopathic medical college Hospital from October 2019 to March 2020.

Method of collection of data:
Patients with Polyarticular Inflammatory arthritis were identified with Diagnostic criteria using specially designed case records from OPD and peripheral clinics. C Reactive Protein and Erythrocyte sedimentation rate were done as baseline investigations.

Study Design: Open label, Pre-test Post- test, quasi-experimental study
Sample size: Thirty diagnosed cases of Polyarticular Inflammatory arthritis according to diagnostic criteria were taken for study. Formal effect size and sample size calculation was not possible on account of under reporting of earlier studies with similar design. However, the sample size was calculated for a population size of 35000 with 2% of hypothesized disease frequency with confidence interval of 95%.
Study type: Interventional study with hydro -ethanolic extract of Stellaria media.
Selection Criteria:
Inclusion Criteria
- Diagnosed case of Polyarticular Inflammatory arthritis with diagnostic criteria
- Age group 18 years to 60 years.
- Male and female sex

Exclusion Criteria
- Patients with any other systemic diseases
- Patients with serious Immunodeficiency diseases
- Patients taking analgesics

Method of Intervention:
0.5 ml of Hydro -ethanolic extract of Stellaria media was mixed with 15 ml of Aqua distillate and taken per oral, two times in a day, after food, for one -month period.
Plan of data Analysis:
Data was analysed using Numeric Pain Rating Scale (NPRS) [10], Erythrocyte sedimentation rate and levels of C- Reactive after one month.
Ethical clearance was obtained from the Institutional Ethical Committee prior to the commencement of study (Ref No: IEC/03/19-20).

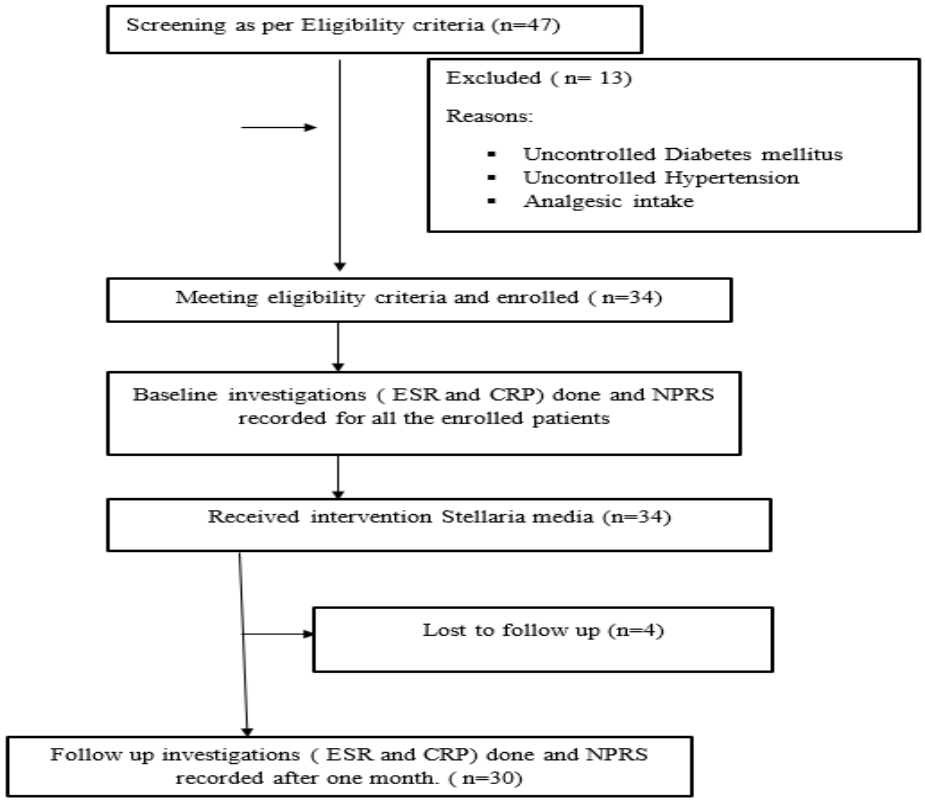

Figure 1. Study flow chart

4.3 Statistical analysis

The results of in-vitro study were expressed as means and standard deviations of the control and treated cells from triplicate measurements (n = 3) of three different experiments. Data were subjected to one-way ANOVA and the significance of differences between means was calculated by Duncan's multiple range test, using SPSS for Windows, standard version 16 (SPSS, Inc.), and significance was accepted at $P \leq 0.05$. The results of clinical study were statistically processed by paired 't' test using SPSS for Windows, standard version 16 (SPSS, Inc.), The null hypothesis (H_0) assumed that there may be no difference before and after the treatment and alternate hypothesis (H_1) assumed that there may be significant difference before and after the treatment.

4. RESULTS

5.1 In – vitro study

Evaluation of Cell viability and cytotoxicity by MTT assay

To evaluate the cell viability, different concentrations of SM (6.25–50µg/ml) was added to hPBMC cells and incubated for 24hrs. There was no significant cytotoxic activity shown by SM in all the tested concentrations. The result showed that the potent dose is 25µg/ml because it showed the highest percentage of cell viability of 92%. The result is shown in the figure 2.

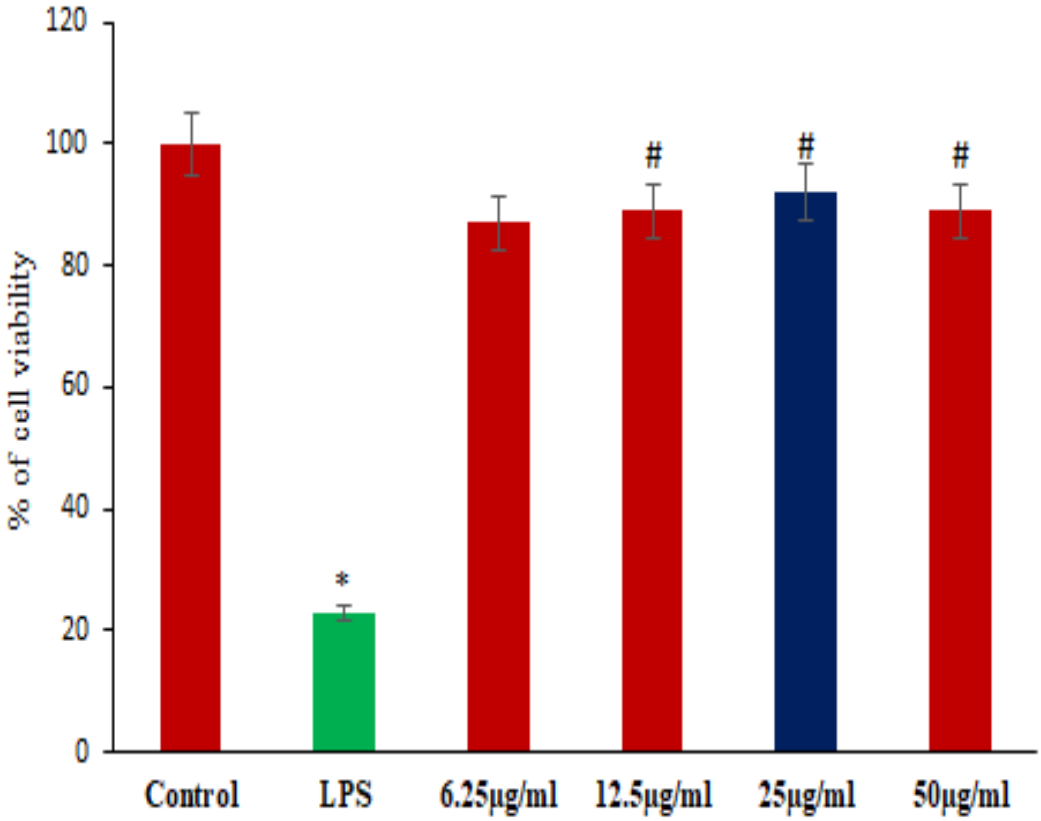

Figure 2. Cell viability assay done by MTT assay. hPBMCs cells were incubated with different concentrations of SM for 24 h.* Compared with control group, $P < 0.05$. # compared with LPS treated group, $P < 0.05$**.** Values are expressed as mean ± SD (n=3).

Morphological analysis of hPBMCs

Morphological analysis of LPS treated hPBMCs showed that the cell size, number of cells was reduced, and shrinkage was also observed. Reduction of cell count is due to cellular necrosis and apoptosis by LPS treatment, but the cells treated with SM help to maintain the normal cell morphology as compared with LPS treated group. There was no shrinkage, apoptosis, necrosis observed in SM treated group and viable and healthy cells were observed as similar to normal group (Figure 3).

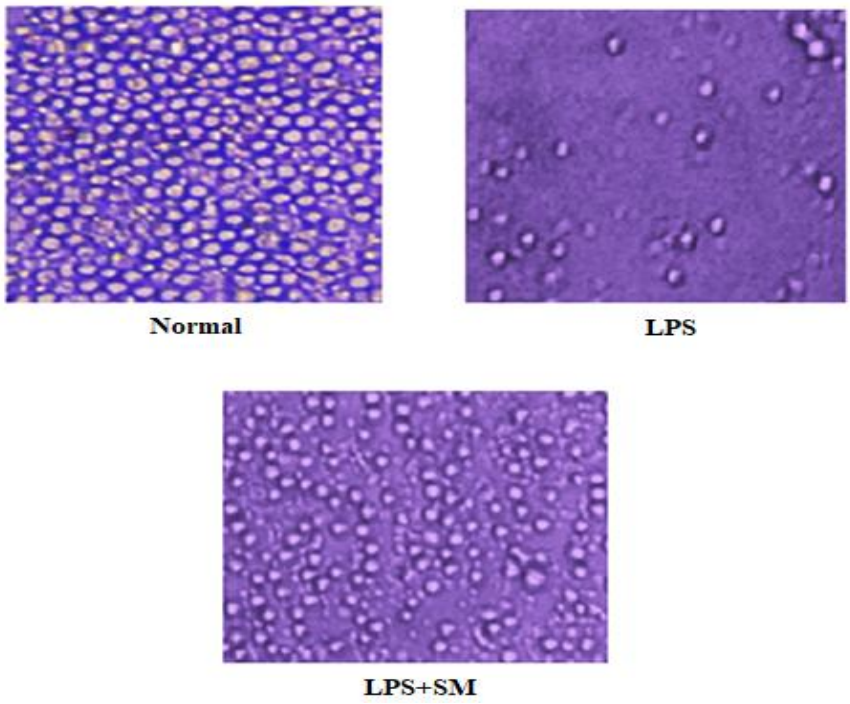

Figure 3. Morphological analysis of hPBMCs

Determination of intracellular ROS generation by using green fluorescence assay

Intracellular ROS can be measured in live cells using DCFDA assay. The result demonstrates that cells incubated with LPS significantly increases ($P \leq 0.05$) the intracellular reactive oxygen species, as compared to the control. SM administration drastically reduced ($P \leq 0.05$) the ROS generation which indicates that it helps to reduce the severe oxidative stress induced by LPS. The result is shown in the figure 4.

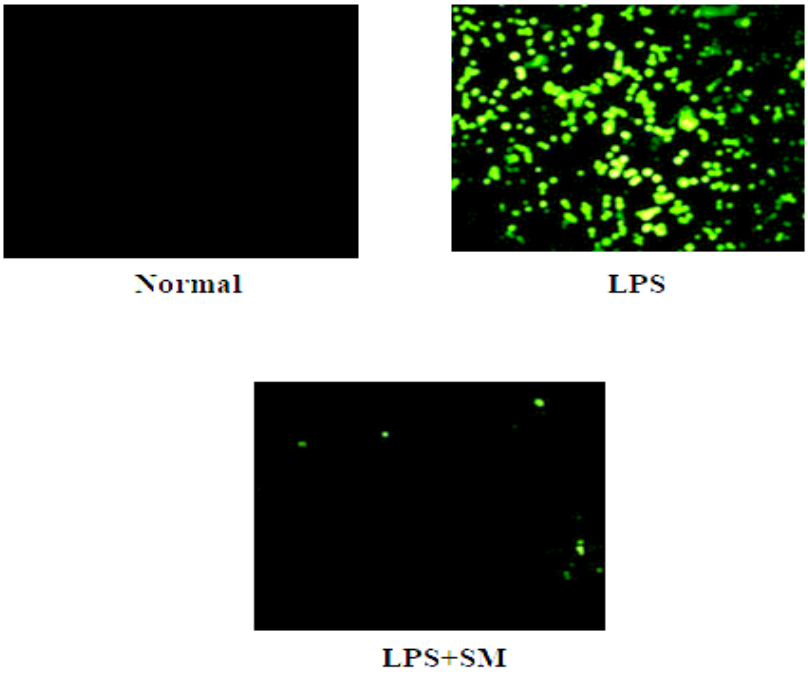

Figure 4. Intracellular ROS generation by using green fluorescence assay.

Effect of SM on COX-2 activity

The concentration of COX-2 was significantly increased in LPS treated group in comparison with normal group. Cells treated with SM showed a significant decrease in the concentration of COX-2 when compared to LPS control group (Figure 5).

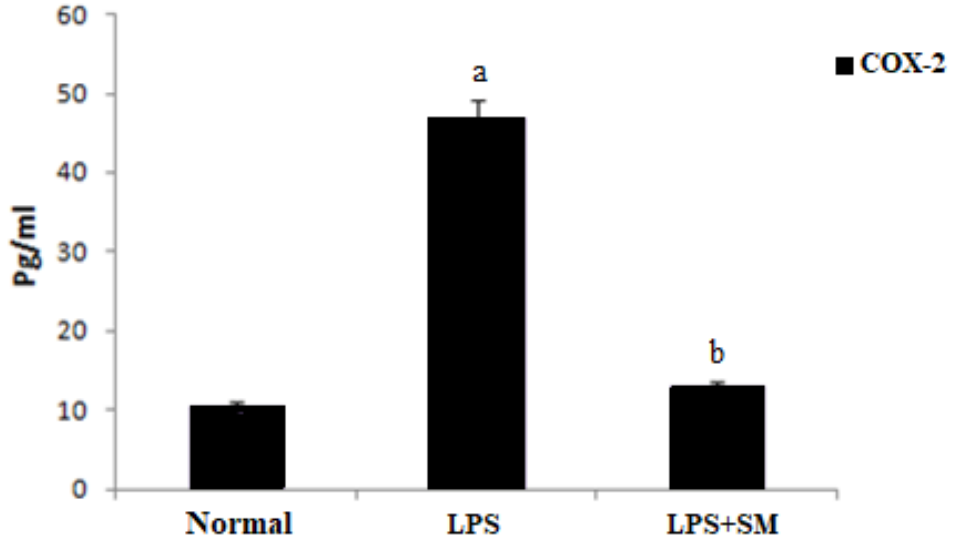

Figure 5. Effect of SM on the COX-2 activity. Values expressed as an average of 3 samples ± SD in each group. 'a' -Statistical difference with normal control group at P < 0.05. 'b' -Statistical difference with LPS treated group at P < 0.05.

Effect of SM in pro-inflammatory cytokines IL-6

In figure 6, shows that IL-6 secretion into the culture supernatant of untreated and LPS treated PBMCs cells, SM treated cells respectively. LPS treatment of PBMCs cells increased cytokine secretion indicated an inflammatory condition. However, when those stimulated cells were treated with SM at 25 µg/ml, the secretion of IL-6 significantly decreased.

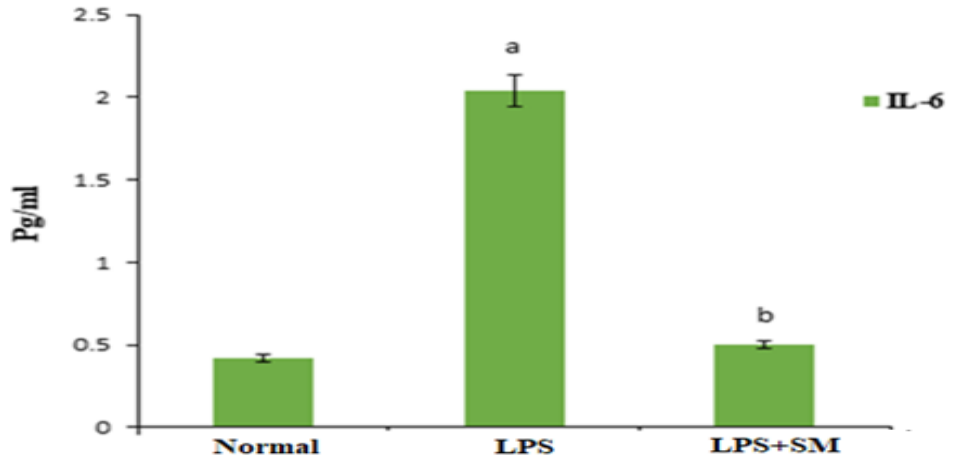

Figure 6. Effect of SM on the IL-6 level. Values expressed as an average of 3 samples ± SD in each group. 'a' -Statistical difference with control group at P < 0.05. 'b' -Statistical difference with LPS at P < 0.05.

5.2 Clinical study

Table 1. Effectiveness of Stellaria media on ESR of patients with Polyarticular arthritis

	Mean (mm/Hr)	SD	N	Mean difference	Paired t	P
Pre-treatment	22.8	8.6	30			
Post- treatment	16.5	5.1	30	6.2	5.6*	0.000

*Significant at 0.05 level.

The average score regarding ESR of patients with Polyarticular arthritis are 22.8 and 16.5 respectively for before and after the intervention with Stellaria media.

The paired t test (t = 5.6, p < 0.05) shows that the decrease in ESR of 6.2 due to the intervention with Stellaria media is statistically significant at 0.05 level.

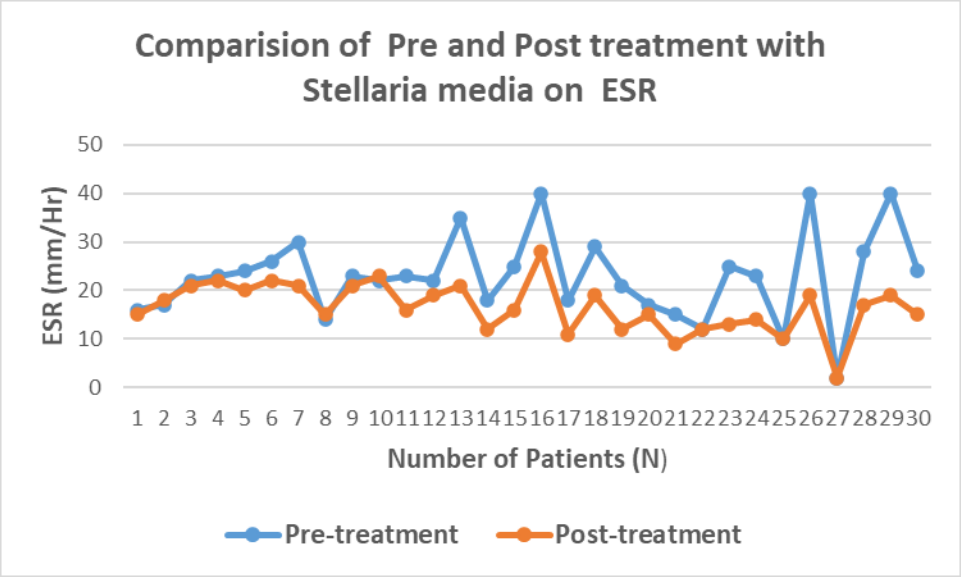

Figure 7. Comparison of Pre and Post treatment with Stellaria media on ESR

Table 2. Effectiveness of Stellaria media on CRP of patients with Polyarticular arthritis

	Mean(mg/dL)	SD	N	Mean difference	Paired t	P
Pre-treatment	3.2	1.7	28			
Post- treatment	2.1	0.7	28	1.02	4.41*	0.000

* Significant at 0.05 level.

The average score regarding CRP of patients with Polyarticular arthritis are 3.2 and 2.1 respectively for before and after the intervention with Stellaria media.
The paired t ($t = 4.41$, $p < 0.05$) shows that the decrease in ESR of 1.02 due to the intervention is statistically significant at 0.05 level.

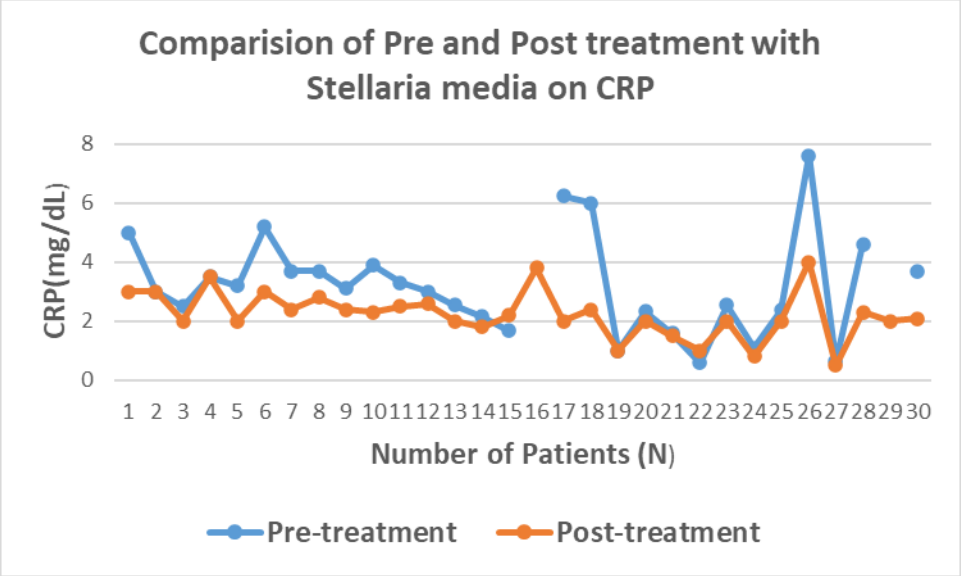

Figure 8.Comparison of Pre and Post treatment with Stellaria media on CRP

Table 3. Effectiveness of Stellaria media on Numerical Pain Rating Scale of patients with Polyarticular arthritis. -

	Mean	SD	N	Mean difference	Paired t	P
Pre-treatment	7.13	1.2	30			
Post- treatment	3.27	0.9	30	3.86	21.76*	0.000

* Significant at 0.05 level.

The average score regarding Numerical Pain Rating Scale of patients with Polyarticular arthritis are 7.13 and 3.27 respectively for before and after the intervention with Stellaria media.
The paired t ($t = 21.76$, $p < 0.05$) shows that the decrease in NPRS of 3.86 due to the intervention is statistically significant at 0.05 level.

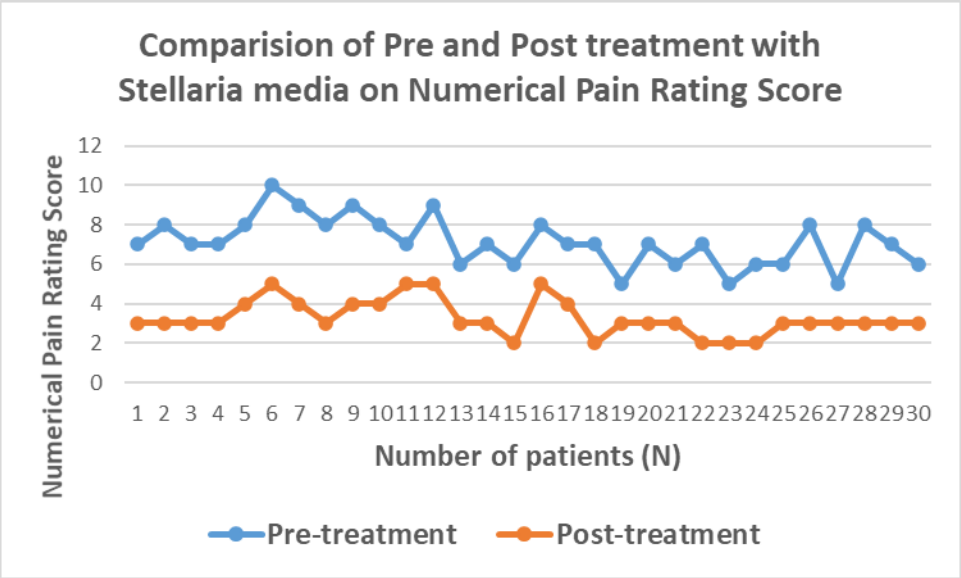

Figure 9. Comparison of Pre and Post treatment with Stellaria media on NPRS

6. DISCUSSION

The inflammatory response is an essential physiological mechanism for tissue protection and repair; however, its dysregulation contributes to the pathogenesis of numerous chronic diseases. [1,2] Lipopolysaccharide (LPS)-activated human peripheral blood mononuclear cells (hPBMCs) are a well-established in-vitro model for investigating the anti-inflammatory potential of therapeutic agents.[11]
In the present study, cell viability analysis using the MTT assay demonstrated that Stellaria media mother tincture (SM) was non-cytotoxic, maintaining 92% viability at a concentration of 25 µg/ml. No adverse morphological changes were observed in SM-treated cells, whereas LPS exposure markedly reduced viability to 23% and induced morphological features consistent with necrosis and apoptosis. These findings confirm the safety of SM at the tested concentrations.[12]
Oxidative stress, driven by excessive reactive oxygen species (ROS), is a major contributor to inflammation.[13] While ROS play physiological roles in immune defence and intracellular signaling, their overproduction can damage lipids, proteins, and DNA, leading to cell death.[14] Using the H2DCFDA probe, we observed a significant reduction in LPS-induced ROS levels following SM treatment, indicating a protective antioxidant effect consistent with previous phytochemical and antioxidant reports on S. media.[5,8]
LPS stimulation is also known to upregulate pro-inflammatory mediators such as interleukin-6 (IL-6) and cyclooxygenase-2 (COX-2) via NF-κB activation (15–17). IL-6 is a pleiotropic cytokine that, when elevated, is associated with a variety of inflammatory disorders[18], while COX-2 upregulation drives prostaglandin synthesis and sustains chronic inflammation.[19] In this study, SM significantly downregulated both IL-6 secretion and COX-2 expression in hPBMCs, suggesting that its anti-inflammatory effect may involve modulation of NF-κB–dependent pathways, aligning with findings from earlier in-vivo studies.[5,7]
The clinical results corroborated the in-vitro findings. Patients treated with SM demonstrated significant post-treatment reductions in ESR, CRP, and NPRS scores, reflecting improvements in joint pain, swelling, and stiffness. These outcomes are in line with the Materia medica indications for S. media, which include sharp shifting rheumatic pains, joint stiffness, synovitis, and localized muscular discomfort.[20] Previous clinical investigations into homoeopathic interventions for arthritis have similarly reported symptomatic improvement without adverse effects.[9]
Nevertheless, certain limitations should be acknowledged. Baseline ESR and CRP values in the study cohort were not markedly elevated compared to NPRS scores, which may have underestimated biochemical treatment effects. The trial duration was shortened to one month due to pandemic-related

constraints, limiting long-term outcome assessment. Furthermore, formal effect size and power calculations were not feasible due to the scarcity of comparable prior studies.

Despite these limitations, the combined in-vitro and clinical evidence indicates that S. media has significant anti-inflammatory and antioxidant potential and may serve as a cost-effective adjunctive treatment for polyarticular inflammatory arthritis. Larger, randomized controlled trials with extended follow-up are warranted to validate these findings and further elucidate the molecular mechanisms involved.

7. CONCLUSION

Both the in-vitro and clinical findings demonstrate that Stellaria media mother tincture exerts significant anti-inflammatory effects, likely mediated through reduction of oxidative stress and downregulation of pro-inflammatory mediators such as IL-6 and COX-2. Clinically, treatment was associated with notable improvements in CRP, ESR, and NPRS scores, suggesting its potential as a cost-effective option for managing polyarticular inflammatory arthritis. Further large-scale, controlled studies with longer follow-up are warranted to confirm these results and elucidate underlying mechanisms.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCE:

1. Harsh mohan, Textbook of Pathology,8th edition, Jaypee brothers medical publishers (P) Ltd, 2018, p.136-138.
2. Porter S Robert, The Merck manual of diagnosis and therapy, 20th edition, Merck Research Laboratories,2018, p.258 -259.
3. Clarke J. H., 'Stellaria media' Dictionary of Practical Materia Medica, B. Jain Publishers, New Delhi, Edition 2000
4. Homoeopathic pharmacopoeia of India, Volume IX, Govt. of India, 2006
5. B.O. Oyebanji, A.B. Saba, O.A. OridupaAnti-inflammatory and analgesic effects of methanol extract of Stellaria media (L.) Vill. Leaf Afr. J. Biochem. Res., 15 (2012), pp. 29-34
6. Antioxidant activity of Silene alba subsp. divaricata and Stellaria media subsp. media from Caryophyllaceae, Turgut Taskin, Leyla Bitis Department of Pharmacognosy, Faculty of Pharmacy, Marmara University, Istanbul, Turke, Published online in ScopeMed (www.scopemed.org). Spatula DD. 2013; 3(1):1-5.
7. Stellaria media (L.) Vill.- A plant with immense therapeutic potentials: phytochemistry and pharmacology. oluwole solomon oladeji, Abel kolawole oyebamiji, Heliyon6(6),e04150, 2020
8. Preliminary Anti-Oxidant Profile of Selected Medicinal Plants of Pakistan Rabia Usman, Arshad Khan, Saira Gul, Abdur Rauf and Naveed Muhammad 1111 2 Institute of Chemical Sciences, University of Peshawar, Peshawar, KPK, Pakistan 1 Departments of Pharmacy, University of Peshawar, Peshawar, KPK, Pakistan
9. Homoeopathic therapy in rheumatoid arthritis: evaluation by double- blind clinical therapeutic trial. RG Gibson, SL Gibson ,AD MacNeill, WW Buchanan.
10. Hawker GA. Measures of Adult Pain. Arthritis Care & Research 2011; 63, S240–S252.
11. Kotas ME, Medzhitov R, Homeostasis, inflammation, and disease susceptibility, Cell, 2015; 160: 816– 827
12. Marshall NJ, Goodwin CJ, Holt SJ. A critical assessment of the use of microculture tetrazolium assays to measure cell growth and function. Growth Regul. 1995; 5: 69–84
13. Wisastra R, Dekker FJ, Inflammation, cancer and oxidative lipoxygenase activity are intimately linked, Cancers, 2014; 6: 1500-1521.
14. McLennan, H. R., Degli Esposti, M. (2000). The contribution of mitochondrial respiratory complexes to the production of reactive oxygen species. Journal of Bioenergetics and Biomembranes, 32(2), 153–162.
15. Castellheim A, Brekke OL, Espevik T, et al, Innate immune responses to danger signals in systemic inflammatory response syndrome and sepsis, Scandinavian Journal of Immunology, 2009; 69: 479–491
16. De Jong HK, Van der Poll T, Wiersinga WJ. The systemic pro-inflammatory response in sepsis. J Innate Immun. 2010; 2: 422–430.
17. Van der Meide PH, Schellekens H. Cytokines and the immune response. Biotherapy. 1996; 8: 243-249.
18. Van Wagoner NJ, Benveniste EN. Interleukin-6 expression and regulation in astrocytes. J Neuroimmunol. 1999;100(1-2):124–139.
19. Debnath T, Hasnat M A, Pervin M, Lee S Y, Park S R, Kim D H, Kweon H J, Kim J M, Lim B O. 2012. Chaga mushroom (Inonotus obliquus) grown on germinated brown rice suppresses inflammation associated with colitis in mice. Food Sci Biotechnol. 21:1235–1241
20. Boericke's New manual of homoeopathic material medica with repertory, B. Jain Publishers, New Delhi, third and augmented edition, 2019, p.536-537