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IMMUNOMODULATORY ACTIVITY OF LEAVES OF *RUMEX VESICARIUS* LINN. AND *SYMPLOCOS RACEMOSA* ROXB.

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Keywords:

Rumex vesicarius Linn., *Symplocos racemosa* Roxb., Carbon Clearance Test, Delayed Type Hypersensitivity test

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ABSTRACT: Objective: To determine the immunomodulatory activity of leaves of *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb. **Methods:** The ethyl acetate and ethanolic extract of *Rumex Vesicarius* Linn. and ethanolic and N-hexane extract of *Symplocos racemosa* Roxb. were administered orally at the dosage level of 200 mg/kg/day and 400 mg/kg/day each according to the body weight of Rat. The assessments of immunomodulatory activity were carried out by using Carbon Clearance Test and Delayed Type Hypersensitivity Test. **Result:** Oral administration of all the extract of *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb. significantly ($P < 0.0001$) showed an increase in phagocytic activity and DTH response in Rat at an experimental dose. The study also comprises the acute toxicity study and preliminary phytochemical screening. **Conclusion:** The study demonstrate that all the extract of *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb. shows the significant immunomodulatory effect on both humoral as well as cell-mediated immunity.

INTRODUCTION: The immune system is a remarkably versatile defense system that has evolved to protect animals from invading pathogenic microorganisms to eliminate the disease. It is able to generate a multifarious variety of cells and molecules capable of specifically recognizing and eliminating variety of foreign invaders [1]. It is now being recognized that modulation of immunological response could provide an alternative to conventional chemotherapy for a variety of diseased conditions of impaired immune responsiveness or when a selective immunosuppression has to be induced in situations like autoimmune disorders and organ transplantation.

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The modulation of the immune response by using Ayurvedic herbal medications as a possible therapeutic measure has now become a subject of scientific investigation. One of the therapeutic strategies in Ayurvedic medicines is to enhance the body's overall natural resistance to the disease causing agent rather than directly neutralizing the agent itself [2]. Immunomodulation is the process of modifying an immune response in a positive (immunostimulation) or negative manner (immunosuppressant) by administration of a drug or compound [3].

There are many plants which are used as immunomodulators. *Heterostemma tanjorense* shows immunostimulant activity against Azathioprine administered rats [4]. The methanolic root extract of *Withania somnifera* shows immunostimulatory activities in dexamethasone induced immunocompromised mice and in vitro model [5]. The Methanolic leaf extract of *Moringa oleifera* shows an immunostimulatory effect on

both the cell-mediated and humoral immune systems in the Wistar albino rats [6]. The methanolic leaf extracts of *Cameroonian* medicinal plants possess immunomodulatory activity [7].The ethanolic extract of *Sonerila tinnevelliensis* showed a stimulatory effect on both humoral and cellular immune functions in animal models [8]. *Caesalpinia sappan* shows the nonspecific immunomodulatory effect on murine peritoneal macrophages [9]. The aqueous leaf extract of *Ocimum basilicum* Linn. is a potent immunostimulant, stimulating specific and nonspecific immune mechanisms. The immuno-stimulatory activity of *O. basilicum* is due to flavonoids (quercetin), alkaloids, tannins, saponin glycosides and phenolic compounds [10].

The methanolic extract of *Trigonella foenum* whole plant has shown significant immunostimulatory activity in various models of Drug-induced myelosuppression [11]. The flavonoids isolated from freshly harvested leaves of *Prosopis spicigera*, *Mimusops elengi* and *Terminalia arjuna* showed dose dependent immunosuppressive activity [12]. The crude terpenoids extract from the leaves of *Emblica officinalis*, *Ficus racemosa and Strychnos nux-vomica* on human whole blood stimulated with hepatitis B vaccine possess immunosuppressive activity [13].

The aqueous extract of *Leucas aspera* was evaluated in cyclophosphamide-induced immunosuppressive mice and it shows prominent immunostimulatory effect [14]. The leaves of *Calotropis gigantea*, *C. rotang* and *A. integrifolia* have an immunosuppressive activity of the variable doses of crude saponin (0.625 – 2.5 mg) on lymphocytes, monocytes and granulocytes [15].

Triptolide, the active component of *Tripterygium wilfordii* can be used alone or in combination with existing therapeutic modalities as novel treatments for autoimmune disorders, cancers, and for immunosuppression [16]. The ethanolic extracts from leaves of *Rhaphidophora korthalsii* stimulate immune cell proliferation, peripheral blood NK cell population [17]. Cyclotides, ribosomally synthesized plant peptides have growth-inhibiting effects on primary cells of the human immune system [18]. The isogarcinol, active compound from *Garcinia mangostana* L. inhibite Calcineurin unique protein phosphatase, plays an important role in immune regulation in a dose-dependent manner [19]. Natural therapies help to regulate the immune system's aggressive behavior without suppressing necessary defenses [20].

For this study we have selected two plants, *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb.

Rumex vesicarius Linn. (Chooka) belongs to perennial herbs to the family Polygonaceae. The plant is an erect usually with a long taproot. Traditionally the plant is used as stomachic, Diuretic, used for the disorders of the lymphatic and glandular system, for bronchitis, asthma, constipation, dyspepsia and the diseases of the liver. Plant leaves are rich in ascorbic acid, citric acid and tartaric acid, it also contains glycoside, alkaloid, flavonoids, tannins and phenolic compounds [21, 22].

Symplocos racemosa Roxb. (Lodhra) belongs to the family Symplocaceae, is a small evergreen tree upto 6 m tall. In traditional system it is mainly used as cardiotonic, antipyretic, antihelmintic and laxative properties. It is beneficial in billow fever, urinary discharge; pharmacologically it is used as antimicrobial, antidiarrhoeal, spasmogenic and heart depressant. The plant mainly contains monomethyl pelargonidin gluocosides, loturidine also contain oxalic acid, phytosterol, ellagic acids and oleanolic acid [23, 24, 25].

MATERIALS AND METHODS:

Plant Material: The fresh leaves of *Rumex vesicarius* and *Symplocos racemosa* Roxb. used in this study, collected at the flowering stage (Month: August - November) from the local area of Sangli and Satara, Maharashtra state, India respectively and authenticated by Botanical Survey of India, Pune, Maharashtra. (BSI/WRC/Iden./2015 dated 4-12-2015)

Extraction: The leaves were separated from fresh stems and dried under shade at room temperature until it becomes completely dry. After drying leaves were subjected to size reduction. The shade-dried coarsely powdered leaves (500 g) were subjected to Soxhlet extraction.

A) *Rumex vesicarius* Linn. leaves were subjected to Soxhlet extraction with 95% ethanol and ethyl

acetate to obtain ethanolic and ethyl acetate extract respectively.

B) *Symplocos racemosa* Roxb. leaves were subjected to Soxhlet extraction with 95% ethanol and N-hexane to obtain ethanolic and N-hexane extract respectively. The extracts obtained were subjected to the Rotary flash evaporator to remove excess of solvent and dried extracts were stored in a cool place in tight pack container for further use.

Animals: All the experiments were carried out using male albino rats of wistar strain. Weight around 150 - 200 gm. The animals are free to access of food and water, and they were housed in a natural (12 h each) light-dark cycle. The animals were acclimatized for at least 5 days to the laboratory conditions before the experiment. The experimental protocol was approved by the institutional animal ethics committee (IAEC/ ABCP/09/2016-17) and the care of laboratory animal was taken as per the guidelines of CPCSEA, the ministry of forests and environment government of India.

Preliminary Phytochemical Screening: All the extracts were subjected to preliminary phytochemical screening using the method described by Kokate, Trease and Evans for the detection of various plants constituents. Test were carried out for the presence or absence of Phytoconstituents like glycosides, flavonoids, saponins, alkaloids, carbohydrates, sterols, phenolic compound and reducing compounds [26, 27, 28].

Drugs and Chemicals: All the drugs and Chemical were of analytical grade while the other drugs were procured from - Levamisole (Johnson and Johnson Ltd.,) Cyclophosphamide (Biochem pharmaceutical industries Ltd.,) Colloidal carbon (Indian ink, Camel India Pvt. Ltd.,).

Selection of doses: Acute Toxicity studies were performed according to the organization for economic cooperation and development (OECD) guideline (425). Form acute toxicity study there was no mortality and physical/behavioral changes showed after administration of all the extract over 14 days at the dose of 2000 and 5000 mg/kg to a different group of rat weight around 150 - 200 gm. The experiments were performed after the experimental protocols had been approved by the institutional animal ethical committee.

Pharmacological Screening: The immuno-modulatory activity is carried out by using Carbon clearance test. (Test for Phagocytosis) and Delayed-Type Hypersensitivity Reaction.

Carbon Clearance Test: (Test for Phagocytosis): Procedure:

- In this test, animals were divided into 11 group comprising 6 animals in each.

TABLE 1: TREATMENT GROUPS OF CARBON CLEARANCE TEST

Groups	Treatment	Dose and route of administration
Group I	Vehicle	10 ml/kg P.O.
Group II	Standard drug (Cyclophosphamide)	50 mg/kg P.O.
Group III	Standard drug (Levamisole)	2.5 mg/kg P.O
Group IV	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-400)	400 mg/kg P.O.
Group V	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-200)	200 mg/kg P.O.
Group VI	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-400)	400 mg/kg P.O.
Group VII	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-200)	200 mg/kg P.O.
Group VIII	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-400)	400 mg/kg P.O.
Group IX	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-200)	200 mg/kg P.O.
Group X	n-hexane extract of leaves of *Symplocos racemosa* Roxb.(NSR-400)	400 mg/kg P.O.
Group XI	n-hexane extract of leaves of *Symplocos racemosa* Roxb.(NSR-200)	200 mg/kg P.O.

- Carbon ink suspension was injected via tail vein to each rat 48 hours after the five days treatment
- Blood samples (25 µl) were then withdrawn from the retro-orbital plexus with mild ether anesthesia at 5 and 15 min after injection of colloidal carbon ink lysed in 0.1% sodium carbonate solution (3 ml).
- The optical density was measured spectrophotometrically at 660 nm.
- The phagocytic activity was calculated using the following formula [29, 30].

$$K = \frac{\text{Log OD1} - \text{Log OD2}}{t_2 - t_1}$$

Where ODI and OD2 are the optical density at time t_1 and t_2, respectively.

Preparation of Carbon Ink Suspension: Camlin ink was diluted eight times with saline and used for carbon clearance test in a dose of 10 µl/gm body weight of rat [31].

Statistical Analysis: The result was expressed as mean value ± SEM. The variation in a set of data has been estimated by performing one-way analysis of variation (ANOVA). Individual comparison of group mean value were done using Dunnet's test. The P value < 0.05, were considered statistically significant.

Delayed Type of Hypersensitivity Reaction:
Procedure:

- In this test, animals were divided into 11 group comprising 6 animals in each.

TABLE 2: TREATMENT GROUPS OF DELAYED TYPE HYPERSENSITIVITY

Groups	Treatment	Dose and route of administration
Group I	Vehicle	10 ml/kg P.O.
Group II	Standard drug (Cyclophosphamide)	50 mg/kg P.O.
Group III	Standard drug (Levamisole)	2.5 mg/kg P.O
Group IV	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-400)	400 mg/kg P.O.
Group V	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-200)	200 mg/kg P.O.
Group VI	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-400)	400 mg/kg P.O.
Group VII	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-200)	200 mg/kg P.O.
Group VIII	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-400)	400 mg/kg P.O.
Group IX	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-200)	200 mg/kg P.O.
Group X	N-hexane extract of leaves of *Symplocos racemosa* Roxb. (NSR-400)	400 mg/kg P.O.
Group XI	N-hexane extract of leaves of *Symplocos racemosa* Roxb. (NSR-200)	200 mg/kg P.O.

- Immunized Rat with 0.1ml of 20% SRBCS in normal saline intraperitoneally on 14th day of the study. On day 21st, animals from all groups get challenge with 0.03 ml of 1% SRBCs in sub plantar region of the right hind paw. Footpad reaction was assessed after 24 hrs *i.e.* on the 22nd day. Increase in foot pad edema was measured with the help of vernier caliper [29].

Antigenic Material:
Preparation of Sheep RBCs: Sheep blood was collected in sterile Alsever's solution in 1:1 proportion, Alsever's solution (freshly prepared) blood was kept in the refrigerator and processed for the preparation of SRBCs batch, by centrifugation at 2000 rpm for 10 min and washing with physiological saline 4 - 5 times and then suspending into buffered saline for further use [31].

Composition of Alsever's Solution:

TABLE 3: COMPOSITION OF ALSEVER'S SOLUTION

Chemicals	Quantity(g/L)
Sodium Chloride	4.2
Sodium Citrate	8.0
Citric acid anhydrous	0.55
Glucose	20.5
Distilled water q.s.	1000 ml

Statistical Analysis: The result was expressed as mean value ± SEM. The variation in a set of data has been estimated by performing one-way analysis of variation (ANOVA). Individual comparison of group mean value were done using Dunnett's test. The P value < 0.05, were considered statistically significant.

RESULT:
Acute Oral Toxicity Study: Acute oral toxicity was carried out by the up-down method. It is found that all extract (EARV, ERV, ESR and NSR) were safe at limit dose 4000 mg/kg and 2000 mg/kg, with no mortality and physical/behavioral changes. 1/10th of this dose *i.e.* 400 mg/kg and 200 mg/kg were used in the subsequent study.

Preliminary Phytochemical Study: The presence of various phytoconstituents of the extract was detected by phytochemical screening. The EARV found to contains Alkaloids, Flavonoids, Tannins, Sterols, Carbohydrate and Vitamin C. ERV contains Alkaloids, Flavonoids, Carbohydrate and Vitamin C. ESR found to contain Cardiac glycoside, Flavonoids, Alkaloids, Tannins and Carbohydrate. NSR contains cardiac glycoside, alkaloids and steroids.

Carbon Clearance Test: Effect of EARV, ERV, ESR, and NSR on the phagocytic activity by the carbon clearance test is shown in **Table 4**. The phagocytic activity of the reticuloendothelial system is generally measured by the rate of removal of carbon particles from the bloodstream. In carbon clearance test EARV, ERV and ESR, treated all groups exhibited significantly high phagocytic index ($P < 0.0001$) when compared with control group. While NSR treated group showed a small increase in their phagocytic index when compared with control group. This indicates stimulation of the reticuloendothelial system.

TABLE 4: RESULT OF CARBON CLEARANCE TEST

S. no.	Groups	Treatments	Dose and route of administration	Phagocytic index (Mean ± SEM)
1	I	Control	10 ml/kg (P.O.)	0.0312±0.0005
2	II	Standard (Cyclophosphamide)	50 mg/kg (P.O.)	0.0206±0.0005****
3	III	Standard (Levamisole)	2.5 mg/kg (P.O.)	0.0573±0.0003****
4	IV	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-400)	400 mg/kg (P.O.)	0.0530±0.0004****
5	V	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-200)	200 mg/kg (P.O.)	0.0492±0.0004****
6	VI	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-400)	400 mg/kg (P.O.)	0.04566±0.0005****
7	VII	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-200)	200 mg/kg (P.O.)	0.0414±0.0003****
8	VIII	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-400)	400 mg/kg (P.O.)	0.0391±0.0003****
9	IX	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-200)	200 mg/kg (P.O.)	0.0363±0.0004****
10	X	N-hexane extract of leaves of *Symplocos racemosa* Roxb. (NSR-400)	400 mg/kg (P.O.)	0.0350±0.0002****
11	XI	N-hexane extract of leaves of *Symplocos racemosa* Roxb. (NSR-200)	200 mg/kg (P.O.)	0.0327±0.0002

Values are expressed as (Mean ±SEM). N = 6 ****P < 0.0001. Statistically significant when compared with control group by ANOVA followed by Dunnett's test.

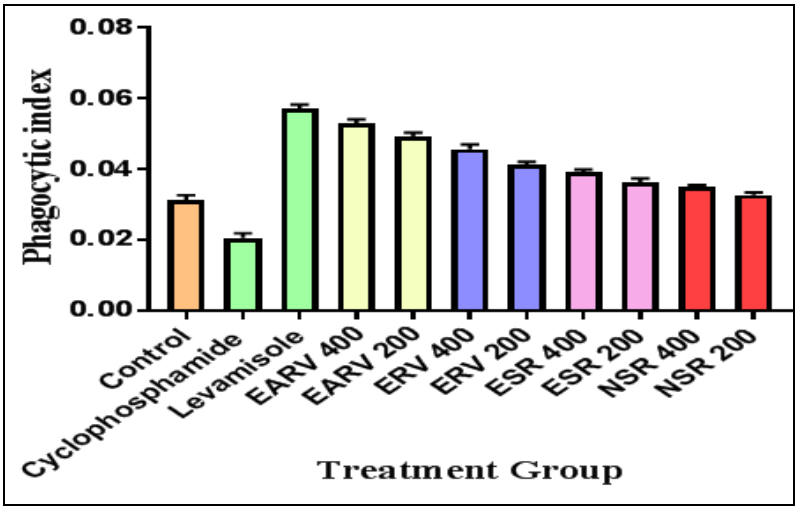

FIG. 1: GRAPHICAL REPRESENTATION OF CARBON CLEARANCE TEST

Delayed Type of Hypersensitivity Reaction: Effect of EARV, ERV, ESR and NSR on the cell-mediated immune response by DTH induce footpad edema is shown in **Table 5**. All treated group EARV, ERV and ESR showed the significantly ($p < 0.0001$) potentiating DTH response in terms of increase in the mean difference of paw edema when compared with control group. It indicates activation of the cellular immune system. While NSR treated group showed a small increase in footpad oedema when compared with control group. Cyclo-phosphamide treated group showed a significant decrease in the mean difference of paw edema when compared with control group.

TABLE 5: RESULT OF DTH

S. no.	Groups	Treatments	Dose and route of administration	Mean Difference in Paw edema (Mean ± SEM)
1	I	Control	10 ml/kg (P.O.)	1.508±0.0316
2	II	Standard (Cyclophosphamide)	50 mg/kg (P.O.)	0.59±0.0513****
3	III	Standard (Levamisole)	2.5 mg/kg (P.O.)	4.56±0.0594****
4	IV	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-400)	400 mg/kg (P.O.)	4.20±0.0545****
5	V	Ethyl acetate extract of leaves of *Rumex vesicarius* L. (EARV-200)	200 mg/kg (P.O.)	3.66±0.123****
6	VI	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-400)	400 mg/kg (P.O.)	3.22±0.0519****
7	VII	Ethanolic extract of leaves of *Rumex vesicarius* L. (ERV-200)	200 mg/kg (P.O.)	2.51±0.0586****
8	VIII	Ethanolic extract of leaves of *Symplocos racemosa* Roxb. (ESR-400)	400 mg/kg (P.O.)	2.29±0.0152****
9	IX	Ethanolic extract of leaves of *Symplocos racemosa* Roxb (ESR-200)	200 mg/kg (P.O.)	2.08±0.0345****
10	X	N-hexane extract of leaves of *Symplocos racemosa* Roxb (NSR-400)	400 mg/kg (P.O.)	1.90±0.0085****
11	XI	N-hexane extract of leaves of *Symplocos racemosa* Roxb. (NSR-200)	200 mg/kg (P.O.)	1.74±0.02986*

Values are expressed as (Mean ± SEM). n = 6 ****P < 0.0001. Statistically significant when compared with control group by ANOVA followed by Dunnett's test.

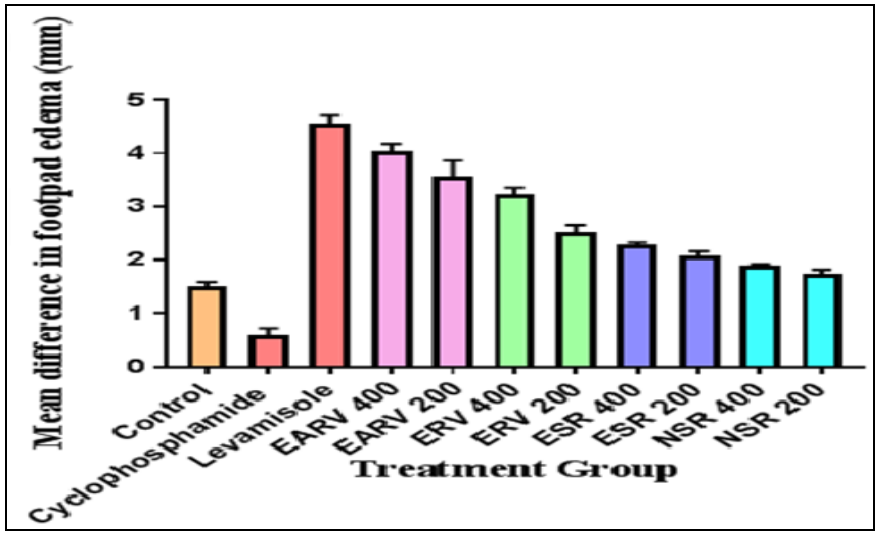

FIG. 2: GRAPHICAL REPRESENTATION OF DTH

DISCUSSION: The immune system is a remarkably versatile system that has evolved to defend itself against a vast range of harmful agents. It is able to generate an enormous variety of cell and molecules capable of specifically recognizing and eliminating a variety of foreign invaders. Immunomodulators are a natural or synthetic substance that helps to regulate or normalize the immune system. Immunomodulators correct immune systems that are out of balance. And immunomodulation is a process which can alter the immune system specifically immunostimulation and immunosuppressant.

The present study was designed to explore the immunomodulatory activity of *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb. In this study Carbon Clearance Test and Delayed Type Hypersensitivity test were selected for evaluation of immunomodulatory activity of *Rumex vesicarius* Linn. and *Symplocos racemosa* Roxb.

According to Smrithi Tripathi *et al*., the Phagocytic activity of reticuloendothelial system was assayed by carbon clearance test phagocytic index was calculated as the rate of carbon elimination of reticuloendothelial system.

In the present study after oral administration of all the extract (EARV, ERV, ESR and NSR) at an experimental dose (400 mg/kg and 200 mg/kg) showed a significant increase in the phagocytic index ($P < 0.0001$) when compared with control group. Increase in phagocytic activity indicates that there was stimulation of reticuloendothelial system.

According to N. L. Dashputre *et al*., Cell-mediated immunity involves the interaction of effectors mechanism carried out by T lymphocytes and their products (lymphokines). DTH required specific recognition of antigen by activated T lymphocytes, which subsequently proliferate and release cytokines. These in turn increase vessel permeability cause vasodilatation, macrophage accumulation, and activation promoting phagocytic activity and increased concentration of lytic enzyme for more effective killing. The delay in the onset of the response reflects the time required for the cytokines to induce the recruitment and activation of macrophages. Therefore increase in DTH response after oral administration of all the extract (EARV, ERV, ESR and NSR) at experimental dose (400 mg/kg and 200 mg/kg) showed a significant increase in footpad edema ($P < 0.0001$) when compared with control. It is indicate stimulation of the cell-mediated immunity.

The Present study revealed that ethyl acetate extract of *Rumex vesicarius* Linn. showed highest immunomodulatory activity.

In this study, the overall order of immuno-modulatory activity was established as EARV > ERV > ESR > NSR.

CONCLUSION: The present study demonstrates that Ethyl acetate and Ethanolic extract of leaves of *Rumex vesicarius* Linn. and ethanolic extract of leaves of *Symplocos racemosa* Roxb. showed significant immunomodulatory effect on both humoral as well as cell-mediated immunity which is due to

- Activation of T-cell which mediated DTH response.
- By the activation of the reticuloendothelial system.
- Enhance the capacity of monocytes Macrophages system.

Further among the all extract (EARV, ERV, ESR and NSR) Ethyl acetate extract of leaves of *Rumex vesicarius* Linn. (EARV) at experimental dose shows more immunomodulatory activity than ERV, ESR and NSR. The overall order of immunomodulatory activity is EARV > ERV > ESR > NSR. A detailed investigation may be carried out to ascertain its exact mechanism of immunomodulatory action.

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CONFLICT OF INTEREST: The authors declare that they have no conflict of interests.

REFERENCES:

1. Mazumder PM, Pattnayak S, Parvani H, Sasmal D and Rathinavelusamy P: Evaluation of immunomodulatory activity of *Glycyrhiza glabra* L. roots in combination with zing. Asian pacific journal of tropical biomedicine 2012; S15-S20.
2. Tripathi JS and Singh RH: The Concept and Practice of Immunomodulation in Ayurveda and the Role of Rasayanas as Immunomodulators. Ancient Science of Life 1999; 19: 59-63.
3. Bagwan SA, Naikwade NS and Manure JY: Review on Immunity and Screening Methods of Immunity. Inventi Rapid: Infectious Diseases and Immunology 2017; 2: 1-13.
4. Manikandaselvi S, Angumeenal AR, Thilagam S, Poornima V and Thinagarbabu R: Immuno stimulant activity of *Heterostemma tanjorense* (Wight and Arn) on azathioprine induced male albino rats. Journal of Applied Pharmaceutical Science 2015; 5: 139-142.
5. Kumari P, Singh SK, Dimrib U, Katariac M and Ahlawata S: Immunostimulatory activities of *Withania somnifera* root extract in dexamethasone induced immuno-compromised mice and *in vitro* model. Asian Journal of Complementary and Alternative Medicine 2014; 2: 6-10.
6. Nfambi J, Bbosa GS, Sembajwe LF, Gakunga J and Kasolo JN: Immunomodulatory activity of methanolic leaf extract of *Moringa oleifera* in Wistar albino rats. Journal of basic and clinical physiology and pharmacology 2015; 6: 603-611.
7. Djafoua YM, Mouokeu RS, Tume C, Kamtchueng MO and Kuiate JR: Immunomodulatory activity of methanol leaf extracts of Cameroonian medicinal plants. Journal of complementary and integrative medicine 2015; 12: 267-275.
8. Tresina PS, Paulpriya K and Mohan VR: Immunomodulatory activities of ethanol extract of *Sonerila tinnevelliensis* Fischer (Melastomataceae) whole plant in mice. The Pharma Innovation Journal 2016; 5: 94-97.
9. Sunitha VS, Sunil MA, Radhakrishnan EK and Mathew J: Immunomodulatory Activity of *Caesalpinia sappan* L. Extracts on Peritoneal Macrophage of Albino Mice. International Journal of Science and Research 2015; 4: 449-452.
10. Nahak G and Sahu RK: Immunomodulatory Activity of Aqueous Leaf Extract of *Ocimum Basilicum* Linn. in

Clarias batrachus. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6: 433-440.
11. Anarthe SJ, Sunitha, Sandhya Rani D and Raju MG: Immunomodulatory Activity for Methanolic Extract of *Trigonella foenum graecum* Whole Plant in Wistar Albino Rats. American Journal of Phytomedicine and Clinical Therapeutics 2014; 2: 1081-1092.
12. Gupta A and Chaphalkar SR: Immunosuppressive activity of flavonoids isolated from *Terminalia arjuna*, *Prosopis spicigera* and *Mimusops elengi*. International Journal of Research in Pharmacy and Science 2015; 5: 14-17.
13. Gupta A and Chaphalkar SR: Immunosuppressive activity of crude terpenoids from extracts of *Emblica officinalis*, *Ficus racemosa* and *Strychnos nux-vomica*. Micromedicine 2016; 4: 1-7.
14. Stalin S and Kumar PS: Immunostimulatory Effect Of Aqueous Extract of *Leucas aspera* in Cyclophosphamide Induced Immunosuppressive Mice. International Journal of PharmTech Research 2013; 5: 910-914.
15. Gupta A and Chaphalkar SR: Immunosuppressive activity of crude saponins from the leaves of *Calotropis gigantea*, *Calamus roteng* and *Artocarpus integrifolia*. International Journal of Pharma Sciences and Research 2015; 6: 526-531.
16. Ziaei S and Halaby R: Immunosuppressive, anti-inflammatory and anti-cancer properties of triptolide: A mini review. Avicenna Journal of Phytomedicine 2016; 6: 149-164.
17. Yeap SK, Omar AR, Ali AM, Ho WY, Beh BK and Alitheen NB: Immunomodulatory Effect of *Rhaphidophora korthalsii* on Natural Killer Cell Cytotoxicity. Evidence-Based Complementary and Alternative Medicine 2012; 1: 1-7.
18. Grundemann C, Koehbach J, Huber R, and Gruber CW: Do Plant Cyclotides Have Potential As Immunosuppressant Peptides? Journal of natural product 2012; 75: 167-174.
19. Cen J, Shi M, Yang Y, Fu Y, Zhou H, Wang M *et al.*: Isogarcinol Is a New Immunosuppressant. PLoS ONE 2013; 8.
20. Zampieron, Eugene R, Kamhi and Ellen J: Natural Support for Autoimmune and Inflammatory Disease. Journal of Restorative Medicine 2012; 1: 38-47.
21. Mathews KM: The Flora of the Tamilnadu Carnatic: Gamopetalae and Monochlamydeae. Rapinat Herbarium, St. Joseph's College, Second Edition 1987.
22. Ghani A: Medicinal Plants of Bangladesh with Chemical Constituents and Uses. Asiatic Society of Bangladesh, Second Edition 2003.
23. Vijayabaskaran M, Badkhal AK, Babu G, Sivakumar P, Perumal P and Sivakumar T: Antitumor Activity and Antioxidant Status of *Symplocos racemosa* Roxb. against Ehrlich Ascites Carcinoma in Swiss Albino Mice. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2010; 3: 306-314.
24. Tiwari RD and Gupta RK: Chemical examination of the bark of *Symplocos racemosa* Roxb. Vijnana Parishad Anusandhan Patrika 1958; 1: 211-214.
25. Mishra SS, Bapat SK and Tewari JP: Preliminary phytochemical and pharmacological study of *Symplocos racemosa* Roxb. Indian Journal of Physiology and Pharmacology 1964; 8: 181-183.
26. Trease GE and Evans MC: Textbook of pharmacognosy. Sunders Elsevier, Sixteenth Edition 2009.
27. Kokate CK, Purohit AP and Gokhale SB: Pharmacognosy. Nirali prahashan, Fifty Second Edition 2016.
28. Khandelwal KR and Sethi V: Practical Pharmacognosy. Nirali prahashan, Twenty Seventh Edition 2016.
29. Tripathi S, Maurya AK, Kahrana M, Kaul A and Sahu RK: Immunomodulatory property of ethanolic extract of *Trigonella foenum-graeceum* leaves on mice. Scholar Research Library 2012; 4: 708-713.
30. Sharma A and Rangari V: Immunomodulatory activity of methanol extract of *Adansonia digitata* L. Tropical Journal of Pharmaceutical Research 2016; 15: 1923-1927.
31. Dashputre NL and Naikwade NS: Immunomodulatory activity of *Abutilon indicum* Linn. On Albino Mice. International Journal of Pharma Sciences and Research 2010; 1: 178-184.

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