The immune system is a network of specialized tissues, organs, cells, and chemical mediators. The immune system comprises of Innate (non-specific) and Adaptive immunity (specific) and other cells like macrophages, natural killer cells. Innate immunity is present at birth and provides the first barrier against foreign entities. The skin, mucus secretions, and the acidity of the stomach are examples of innate immunity that act as barriers to keep unwanted agents away from more vulnerable tissues. Adaptive immunity is the second barrier to infection. It is acquired later in life. The adaptive immune system retains a memory of all the invaders it has encountered and become activated after an attack from the same invader. Antigen Presenting Cells (APCs) are involved in the fighting against antigens. These antigens could be (fungi, viruses, bacterial toxin) which are processed by APC’s presented to T-cells for further processing. Phagocytic cells which are involved in immune system are neutrophils, basophills, eosinophills and monocytes; they engulf and destroy the antigens or foreign substances with their intra cellular mechanisms.

Many of the plant products exert some effect on immune system. They either enhance immune response to help body clear undesirable agents from body or suppress immune response to control deterioration in the body. Compounds that alter immune response are considered Immunomodulatory agent.

Immunomodulation is the regulation and modulation of immunity either by enhancing or by reducing the immune response. Modulation of immune response may involve induction, expression or amplification of immune response. In other words, immunomodulation involves a change in the human body’s immune system caused by agents that activate or suppress its function. If the modulation in immune system results in enhancement of immune reaction, it is known as the immunostimulation. There are two main categories of immunostimulators. The specific immunostimulators are those which provide antigenic specificity in immune response, such as vaccines or any antigen; the non-specific
immunostimulators are those which act irrespective of antigenic specificity to augment immune response of other antigens or stimulate components of the immune system without antigenic specificity, such as adjuvants and non-specific immunostimulators.

For immunomodulatory studies, the whole plant of *Leptadaenia reticulata* (aerial part) was collected in the summer season from the botanical garden of Department of Botany, Dr. Harisingh Gour University, Sagar (M.P.) India and the fruit of *Momordica dioica* was collected during rainy season from the forest of Sagar and Damoh. Both plants were identified and authenticated by the taxonomist of Department of Botany, Dr. Harisingh Gour University, Sagar (M.P.), India and voucher specimen was deposited in institutional herbarium. After due authentication, fresh plant materials were washed, shade dried for a day and then dried completely. The plant materials were coarsely powdered using a rotary grinder and stored in airtight plastic containers. This powder was used for all phytochemical analysis. Crude aqueous and ethanolic extracts of both plants were prepared and used for immunomodulatory studies on Swiss balb-c mice.

*Leptadaenia reticulata* (family Asclepiadaceae) is a climber found in forests and gardens near thorny trees. *L. reticulata* known as the source of the drug and real Jivanti. *Leptadaenia reticulata* well known for its tonic, restorative and stimulant property in the Indian system of medicine.

Crude aqueous extract of *Leptadaenia reticulata* showed significant immunostimulant activity in carbon clearance test by increasing phagocytic index in a dose dependent manner. Crude aqueous extract, increased the phagocytic index significantly. The crude ethanolic extract also enhanced the phagocytic index in dose depended. Increase in phagocytic index indicates that phagocytosis is increasing. Stimulation of phagocytosis is influenced by the activation of macrophages; the activated macrophages secrete a number of cytokines, which in turn
stimulate other immune cells. In the same experiment a dose of 50mg/kg b. wt of crude aqueous extract did not show any significant increase or decrease in the phagocytic effect. This suggests that the active substance, which stimulates the immune system, either is absent or present in such a low concentration that no invocation to phagocytes is generated significantly.

Delayed Type Hypersensitivity Test was done to study the effect for crude aqueous and crude ethanolic extract on cell-mediated immune response to paw edema in 24, 48 hrs and then after 72 and 96 hrs paw volume significantly decreases when compares with control. The reduction in paw volume may be because of a quick action of various enzymes, hormones etc on the invader, simultaneously phagocytosis increase because of activated macrophages and hence reduction in paw volume was observed. Reduction in paw volume after 24 hr. and onwards point to the fact that saponins and similar compounds increase the metabolic activity of the neighboring cells to release metabolites and activated macrophages eliminate the causative agents hence the edema gradually reduces. The increase in paw volume, in response to infiltration of CD4 line of T-lymphocytes and as usual diapedesis of mononuclear macrophages and liberation of edema causing substances for example serotonin, prostaglanddulin E, cytokines etc. The infiltration of lymphocytes is possibly become of the compounds, which perhaps observed the cell-mediated immune response. Extract of *Leptadaenia* having potent activity to involve cell- immune response. This indicates that aqueous extract and ethanol extract contain amines and multiple hormonal substance stimulators like lymphokines. These hypersensitive responses particularly by attracting and activating macrophages. A increase in humoral immune response was observed. Agglutination titer to SRBC fraction also showed agglutination titer up to the same level. Aqueous extract of the plant contained proteins, oligosaccharides and their conjugated compound besides β-sterols, saponins, flavonoids, flavones etc. the antigenicity to elicit antibodies of first two compounds is
well known, but ethanol soluble fraction is devoid of some compounds, other compounds are equally potent for the synthesis of immunoglobulins. Red blood cell at neutral pH possesses negative ions that form cloud, which repel one another Immunoglobulins like IgM can overcome the electric barriers and get cross-link with red blood cells, this leads to subsequent agglutination. From the above results it is possible that there is an enhancement in the level of IgM and IgG because antibody tire against SRBC were raised.

The crude ethanolic extract showed a decrease in the agglutination titer. Crude ethanolic extract at the doses of 100, 150mg/kg b. wt. showed agglutination titer only up to X: 40 and the ethanolic extract suppresses humoral immune response and interfere with antibody formation so less antibody is formed insignificantly, affects agglutination titer against SRBC titer. The study of the results depict that the ethanolic extract surprisingly show almost no change in agglutination titer, perhaps the amount of the compounds that can invoke antibody synthesis is not enough to incite T4 and B lymphocytes or such compounds are not in the extract. This cannot be ignored that immunosupperession may be caused by the other contents of the extract.

Cyclophosphamide suppresses humoral, cellular, non-specific and specific cellular immune response. When animal was treated with cyclophosphamide haemoglobin (Hb), RBC counts, WBC count, Lymphocyte% and Platelet count all are reduced. The suppressive effect of cyclophosphamide was protected by the administration of aqueous extract and their ethanol soluble and ethanol insoluble fraction. Flavonoids in biological systems tend to adhere with the molecules of cyclophosphamide this causes to increase the size of the molecules and prevent its entry to the stem cells. As already stated that such compounds are detected in the plant extract of the besides this some more compounds are there as it can be assumed which are not only negating the effect of cyclophosphamide, but also accelerating the total WBC and hemoglobin count. The crude ethanol extract did not make
any significant elevation in the hematological parameters taken for study on the other hand crude aqueous extract of 100, 150 mg/kg b.wt. showed significant increase in the haemoglobin, RBC count, WBC count; Lymphocytes and platelet count in a dose dependent manner. This suggests that the constituent of the plant preventing the access of cyclophosphamid to the stem cells so that synthesis of haemoglobin, WBC and RBC is not inhibited. Another point is that the compound as are reutilizing this immunosuppressant before it could act upon haemopoeitic and myeloid tissue and its effective amount is present in 100/150 mg of extract. The crude aqueous extract also enhances the number and activates of various immune cells and protects the animal form the adverse effect of cyclophosphamide. On the other hand crude ethanolic extract of *Leptadaenia* showed a mixed effect, sometimes the values of blood parameters increase or decrease. The ethanolic extract showed a dual nature, stimulatory as well as suppressive effect. In some case extract protects the animal from the effect of cyclophosphamide but at certain doses of the extract only it shows a slight reduction in the given values. In addition to carbohydrates, glycosides and saponins, proteins also contribute to a larger extent to immunostimulation more activity to aqueous extract as compare to ethanolic extract.

Cytokines are essential mediators of cell-to-cell signals in physiological and pathological immune responses and in the inflammatory response. Under normal conditions, these cytokines act as crucial signals in the development of appropriate defenses. However, exaggerated or prolonged release can lead to pathological conditions. Both crude aqueous and ethanolic extract enhanced IL-2 levels in a dose dependent manner while the IL-6 showed almost stable levels.

*Momordica dioica* Roxb. (Cucurbitaceae) is commonly known as a bitter gourd. It is traditionally used as astringent, febrifuge, antiseptic, antihelmintic, spermicidal. Also Used in bleeding piles, urinary infection and as a sedative. Studies indicate that it possesses antioxidant,
hepatoprotective, antibacterial, anti-inflammatory, anti-lipid peroxidative, hypoglycemic and analgesic properties.

*Momordica dioica* increases the rate of phagocytic index with respect to control. It was observed that crude aqueous extract and crude ethanolic extract enhance the phagocytic index significantly. Increase in phagocytic index is suggestive of activation of WBC. Increase was dependent on the dose in the case of crude aqueous extract, as the dose increase phagocytic index also increases. Results of these studies clearly indicate that *Momordica dioica* activates the process of phagocytosis. The extract influences the role of neutrophils, digestive enzymes in phagocytic vesicle, and the synthetic processes in the cytoplasm. In treated animal, hyper granulation of WBC is the evidence of it. The secretary material appeared in the cytoplasm is to meet the necessity of the cell to phagocytose and digest the antigen. Stimulation of phagocytosis was influenced by the activation of macrophages, these activated macrophages secrete and number of cytokines such as IL-1, IL-2, etc and that in turn mobilize the immune cell. Aqueous as well as ethanolic extract significantly influenced and activated microphages. *Momordica dioica* has saponins, flavones and other compounds as it is mentioned earlier the compound in this plants have different Rf values hence, their chemical composition would be slightly different and so also their effects on the body. The comparative effects of the extract on phagocytosis vary. The mode of action of the compounds on FCRIII, CRb and CRBi may vary in intensity and the same may be in case antibody and the complement proteins. It is obvious that some of the constituents have definite effect on myeloid tissue directly or through interleukins.

Both the extracts influenced T-Cell activity significantly which in turn increase vascular permeability induce vasodilatation, macrophage accumulation and activation, and which finally result in the increase in the paw volume which promotes phagocytic activity and also increase the concentration of lytic enzymes for more effective killing, this ultimately results in reducing the paw volume after 72 and 96 hrs. Crude ethanolic
extract did not make any significant increase. Since it may contain lesser amount of immunostimulating agents or having some other compounds, which may be partially antagonizing the stimulator. Increase in DTH reaction in mice in response to SRBC revealed the stimulatory effect to aqueous and ethanolic extract on T- lymphocytes and accessory cell types. The results reported here also in conformation it can be opined that the contents present in *Momordica dioica* are much more effective and efficient enough to attract CD4 population of I lymphocytes, monocytes and other lymphocytes.

The humoral immunity involves interaction of B cells with the antigen and their subsequent proliferation and differentiation into antibody secreting cells. Antibody functions as the effectors of the humoral response by binding to antigen and neutralizing it or facilitating its elimination by cross linking to form latex that are more readily ingested by phagocytic cells. Aqueous and ethanolic extracts of *Momordica dioica* increase the agglutination titer to SRBC (antigen). In crude aqueous extract agglutination titer increase, as increase in the dose. Crude ethanolic extract did not show any significant increase in the agglutination titer as compared to control. On the other hand crude aqueous extract showed maximum increase the agglutination titer at the dose of 150 mg/ kg. b. wt. with this dose the agglutination was observed up to serum dilution of X: 320. The crude ethanolic extract showed increase in agglutination titer at the dose of 150 mg/ kg. b. wt. The titer was observed up to the serum dilution of X:160. This indicates the enhanced responsiveness of macrophages and T and B lymphocyte subsets involved in antibodies formation which gives higher agglutination titer sheep red blood cells.

*Momordica dioica* antagonizes the myelosuppressive effect induced by cyclophosphamide, which produces significant myelosuppression in experimental animal. By the administration of cyclophosphamide haemoglobin, RBC count, WBC count. Lymphocyte, monocytes, Eosinophills count and platelet count decrease significantly. But with the
treatment of aqueous and ethanolic extract many of the above parameters increase. This indicates the protection produced by the drug against cyclophosphamide. In the case of crude ethanolic extract increase was observed in a dose dependent manner but it was not significant in each case. Natural product like polypeptides, oligosaccharides, proteoglucons, saponins, flavonoids etc are some of the compounds which are reported to be responsible for the genesis of antibodies still few of them are also to negate the toxic effect of chemicals on haemopoietic tissue, myeloid and lymphoid tissue even some them both qualities observed with *Momordica dioica*. The compound (s) through the path way ultimately activates B- lymphocytes devoid to form plasma cell, which in turn release particular type of antibodies. Appearance of some thicker protein bands during electrophoratic separation, increase in serum protein concentration and high titer for SRBC strongly indicate about humoral immunity stimulation. Cyclophosphamide is known myelosupperssant agent causes to decrease immunology parameters but some compounds of the extract reduce the toxic effect or the components of the extract prevent the entry of cyclophosphamide or bind with this compound to make is insoluble or unite to form a molecule to bind receptor site to wash away the effect of the compound in an short period, *Momordica dioica* thus effective in both ways, to stimulate the immune system and to protect it from immunosupressants.

The electrophoretic pattern of drug treated animal is almost similar to that of serum proteins electrophoretic pattern of control. Both the extracts of both the plants did not elicit any response for the formation of new serum protein. Possibly the technique may not be show much sensitive to detect the new protein which appeared in very little concentration in blood as the constituents of the extracts did not produced new protein. This cannot be ignored that the constituents of both the plants exhibited a definite immunostimulatory effect as evidence by various parameters for immunostimulation increased phagocytic
index and SRBC test go in favour of the drugs for immunostimulation. The increased concentration of serum protein (The reading are not incorporated here) also points to the fact that the liver and probably the plasma cells also produced to increase the concentration of serum protein. Serum of the drug treated animal showed a more darkened spots in comparison to that of control. This shows that the constituents of the drug having effects either on liver are on B lymphocytes and plasma cells.

The qualitative analysis of IL-2 in both control and experimental animals was assessed and correlated with significant increase in WBCs count/lymphocyte count in experimental animals. So for IL-6 is concerned its increase can be correlated with increase paw volume. The cytokines whenever increase in very low concentration a definite effect is produced. These low molecular weight proteins activate the receptors on lymphocytes to cure these sensitivity a growth and activity. IL-2 also stimulates other cellular effectors like GCFs and GMCSF although these factors are not estimated but an indirect conclusion about their increase can be made which inhibits WBCs count and paw edema test. Probably the glucosteroids and flavones which are present in good quantity in the extracts, they are directly or indirectly responsible to elevate the cytokines.

*In vivo* and *in vitro* studies the some herbs do suggest that the immunomodulating effects of the botanical medicines, at least in part, to cytokine modulation. Furthermore, the broad-spectrum effect of cytokines on cell-to-cell communication, it seems likely some of the other organ systems and tissue effects of the herbal immunomodulators are due to modulation of cytokine expression. Both crude aqueous and ethanolic extracts enhanced IL-2 levels in a dose dependent manner while the IL-6 showed almost insignificant increase in its levels.

Finding of these studies on both plant suggest that the both the extracts are capable to strengthen the immune system. Both the extract
modulate immune responses significantly as they increase the phagocytic index, modulate the phagocytic functions of macrophages and phagocytes, which means they have a profound effect over the innate immunity. They also modulate the function of cytotoxic T-cell that produces delayed type hypersensitivity immune response, which gives a better protection against viruses and tumors. They also increase the antibody titer, which means modulation of humoral immunity.