

IMMUNITY, NUTRIENTS AND IMMUNOMODULATION

R. S. Chauhan and Tuls Devi*

Department of Pathology, College of Veterinary and Animal Sciences
G B Pant University of Agri. & Tech. Pantnagar-263145 Uttarakhand,

*PhD scholar, Shri Venkateshwara University.

Abstract

During the process of evolution, nature has provided a unique preventive mechanism known as immune system in each and every living beings. In higher animals and man, the immune system takes care of any extraneous intrusion in the body through its several mechanisms including natural or para-specific immunity, acquired or specific immunity, humoral immunity, cellular immunity etc. However, in the era of modernization, man has introduced several chemicals in the environment through agriculture, animal husbandry and public health operations besides industrialization, urbanization and chemicalization of agriculture. These chemicals normally are used for the control of insects, pests, infections and as preservatives, coloring agents and flavouring agents etc. But inadvertently, these chemicals accumulate in the eco-system and contaminate food chain. Through food chain, these chemicals enter in the body of human beings and animals and affect immune system adversely. During last several years, it has been observed that the pollutant in the environment including pesticides, heavy metals and mycotoxins cause immunosuppression/ immunodeficiency, hypersensitivity/allergy and/or autoimmunity. When there is immunosuppression in the body, the individual becomes susceptible to many kinds of infections and cancers. In such individuals, the drugs including antibiotics may also not be very effective due to failure of phagocytic mechanism. In order to enhance the immunity, several nutritional factors, microbial products, herbs and Cowpathy based products can be used to enhance the immunity. Through the use of these products, the immunity level of an individual is increased to an optimum level so that it will refract any kind of infection or disease and as such an individual will remain protected. However, if at all infection sets in an individual in spite of the above supplementation, it will remain very light and will not harm the body seriously. Such immunomodulatory products are for the control of each and every kind of infectious diseases while the available vaccines are cause specific and are protecting only a single or such disease for which it is used. These products will enhance the immunity non-specifically just to protect any kind of infection.

Key words: Immunity, Immune response, Nutrients, Microbial products, Herbal products, Cowpathy, Immunomodulation.

Introduction

Animals and man require diets balanced in essential nutrients to achieve best growth, reproductive efficiency, feed conversion and immune response against diseases. Deficiencies of proteins and other nutrients like amino acids, minerals, vitamins, etc. may depress the immune system leading to poor response to vaccines and makes animal more susceptible to various infectious diseases. Immunity is the resistance of body against extraneous etiological factors of disease, which is afforded by the interaction of chemical, humoral and cellular reactions in body. This is an integral part of the body without, which one cannot think of life. During the process of evolution, nature has provided this defense mechanism in body of all living creatures particularly of higher animals and man that protects them from physical, chemical and biological insults. It can be classified as natural or paraspecific and acquired or specific immunity.

1. Natural/ paraspecific immunity

There are some species resistant for a particular disease due to presence of natural resistance against them e.g. Horse, pig; chickens are resistant to anthrax. Even within species, there is natural resistance that protects some individuals while others are susceptible e.g. Indian Deshi cattle Zebu (*Bos indicus*) is quite resistant to piroplasmiasis in comparison to *Bos taurus*. Besides, there are the mechanisms or barriers in body provided by nature, which are: *Skin and mucous membrane* prevent organisms from gaining entrance in body, *Mucous* prevents from infections by trapping and keep them away, *Saliva, gastric juice and intestinal enzymes* kill bacteria, *Tears, nasal and GI tract secretions* are bactericidal due to presence of lysozymes, *Phagocytic cells* such as neutrophils kill bacteria through phagocytosis, *Macrophages* kill organisms through phagocytosis, *Natural antibodies* acts as opsonins helps in phagocytosis and *Interferons* have antimicrobial properties. They are host/species specific and arrest the viral replication. *Interleukins, cytotoxins and growth factors* stimulate the immune reactions and inflammation while the *Natural killer cells* kill targets coated with IgG.

2. Acquired/specific Immunity

Acquired immunity develop in body as a result of prior stimulation through antigen. It is specific to a particular antigen against which it was developed. It can be re-stimulated on second or subsequent exposure with antigen and thus, it has memory for a particular antigen. It differs from natural immunity in respect of prior stimulation, specificity

and memory. It can be classified as humoral and cell mediated immunity. The immunity present in fluids of body mainly in blood. There are antibodies in serum of blood, which protect body from diseases. It is specific to particular antigen. Antibodies are formed in blood as a result of exposure of the foreign substances including bacteria, virus, parasite and other substances.

Antigen is foreign substance, which is able to stimulate the production of antibodies in body. They may be of high molecular weight protein, polysaccharides, and nucleic acids. Simple chemicals of low molecular weight are not able to induce immunity. However, they may be conjugated with a large molecular weight molecules such as protein then they become antigenic and induce antibody production, such substances are termed as **haptens**.

Antibodies are protein in nature present in serum and produced as a result of antigen. Antibodies are specific to antigen. Most of the microorganisms have several antigenic determinants and antibodies are produced against each antigenic determinant specifically. The antibody response to antigen can be enhanced if the antigen is released slowly in body. There are several substances like oils, waxes, alum, aluminium hydroxide, which may be added with antigen so that it is released slowly in body to increase the antibody production. Such substances are known as **adjuvants**. Antibodies are also known as **immunoglobulins** as they are the part of globulins. They are glycoprotein in nature and are of 5 types IgG, IgA, IgM, IgD and IgE.

- i. **Immunoglobulin G (IgG):** It is the main antibody found in high concentration (75%) in serum with a mw 150 KD. It is produced by plasma cells in spleen, lymphnodes and bone marrow. It has two identical light chains and two gamma heavy chains. The light chains may be of kappa or lamda type. IgG is the smallest immunoglobulin which may pass through blood vessels with increased permeability. It has the capacity to quickly bind with foreign substances leading to opsonization. Its binding with antigen may also activate the complement.
- ii. **Immunoglobulin M (IgM):** This is about 7% of total serum immunoglobulins. It is also produced by plasma cells in spleen, lymphnodes and bone marrow. It is pentamer, five molecules of conventional immunoglobulin with mw 900 KD. These five molecules are linked through disulfide bonds in a circular form. A cysteine rich polypeptide of 15KD mw binds two of the units to complete circle and is known as 'J' chain. It is produced in body during primary immune response. It is considered to be more active than IgG for complement activation, neutralization of antigen, opsonization and agglutination. IgM molecules are confined to the blood and have no or little effect in tissue fluids, body secretions and in acute inflammation.
- iii. **Immunoglobulin A (IgA):** It is secreted as dimer (mw 300 KD) by plasma cells present under body surfaces like intestinal, respiratory and urinary system, mammary gland and skin. Its concentration is very little in blood. IgA produced in body surfaces is either secreted on surface through epithelial cells or diffuse in blood stream. IgA is transported through intestinal epithelial cells having a receptor of 71 KD which binds with the secretory component covalently to form a secretory IgA. This secretory component protects IgA in the intestinal tract from digestion. It cannot activate the complement and cannot perform the opsonization. IgA can neutralize the antigen and agglutinate the particulate antigen. IgA prevents adherence of foreign particles/antigen on the body surfaces and it can also act inside the cells. It is about 16% of total immunoglobulins present in serum.
- iv. **Immunoglobulin E (IgE):** It is also present on body surfaces and produced by plasma cells located beneath the body surfaces. It is in very low concentration in serum. It can bind on receptors of mast cells and basophils. When any antigen binds to these molecules, it causes degranulation from mast cells leading to release of chemical mediators to cause acute inflammation. It mediates hypersensitivity type I reaction and is responsible to provide resistance against invading parasitic worms. It is of shortest half life (2-3 days) and thus is unstable and can be readily destroyed by mild heat treatment. It is 0.01% of total immunoglobulin in serum with 190 KD molecular weight.
- v. **Immunoglobulin D (IgD):** IgD is absent in most domestic animals. However, it is present in very minute amount in plasma of dog, non human primates and rats. IgD can be detected in plasma. However, it can't be found in serum due to lysis by proteases during clotting. It is only 0.2 % of total immunoglobulin in serum with mw 160 KD.

3. Immune response

The antigen when enters in body of animal is trapped, processed and eliminated by several cells including macrophages, dendritic cells and B-cells. There are two types of antigen in body i.e. exogenous and endogenous. The exogenous or extra cellular antigens are present freely in circulation and are readily available for antigen processing cells.

The endogenous or intracellular antigens are not free and are always inside the cells such as viruses. But when these viruses synthesize new viral proteins using biosynthetic process of the host cells, these proteins also act as antigen and are termed as endogenous or intracellular antigens.

The processing of antigen by macrophages is comparatively less efficient as most of the antigen is destroyed by the lysosomal proteases. An alternate pathway of antigen processing involves antigen uptake by a specialized population of mononuclear cells known as **dendritic cells** located throughout the body specially in lymphoid organs. Such dendritic cells have many long filamentous cytoplasmic processes called dendritic cells and lobulated nuclei with clear cytoplasm containing characteristic granules.

Antigen presenting cells process the exogenous antigen and convert into fragments to bind with MHC class II molecules. Such processed antigen along with MHC class II molecule and certain cytokines such as IL-1 is presented to antigen recognizing cells (T-helper cells). Macrophages also regulate the dose of antigen to prevent inappropriate development of tolerance and provide a small dose of antigen to T- helper cells. However, if the antigen is presented

to T-Cells without MHC class II molecule, the T cells are turned off resulting into tolerance. On an average, an antigen presenting cell possesses about 2×10^5 MHC class II molecules. A T-cell require activation by 200-300 peptide- MHC class II molecules to trigger an immune response. Thus, it is estimated that an antigen-presenting cell may present several epitopes simultaneously to T-helper cells. A counterpart of T- helper cells also exists and known as suppressor T-cells (T_s cell) which suppresses the immune response. The viral encoded proteins, endogenous antigens are handled in a different manner from exogenous antigens. Such antigens are bound to MHC class Ia molecules and transported to the cell surface. Such antigen and MHC class Ia molecule complex triggers a lymphocytic response *i.e.* T-cytotoxic cells (T_c -cells). These cytotoxic T-cells recognize and destroy virus infected cells. However, there is some cross priming leading to cell mediated immune response by exogenous antigens and humoral immune response by endogenous antigens. Some lymphocytes also function as memory cells to initiate secondary immune response. On antigen exposure, there is a latent period of about four to six days and only after that serum antibodies are detectable. The peak of antibody titre is estimated around 2 weeks after exposure to antigen and then declines after about 3 weeks. During this primary immune response, majority antibodies are of IgM type where as in secondary immune response, it is always predominated by IgG.

IMMUNOMODULATION

Immunomodulation is the manipulation of the immune system; it may augment or decrease the magnitude of immune responsiveness. The augmentation of immune response is known as immunostimulation/ immunopotentiality while suppression of immune responsive-ness is termed as immunosuppression. The necessity of suppression the function of the immune system is well recognized in the areas of transplantation and immunopathological disorders like autoimmunity. Conversely, augmentation of immune response has been a matter of much interest among the scientists of veterinary as well as medical sciences in order to increase the host's resistance to disease. Specific immunomodulation is limited to a single antigen such as vaccines *i.e.* immunopotentiality has been for development of resistance in body against a particular disease. Non-specific immunomodulation implies for a more generalized change in immune responsiveness leading to altered host reactivity to many different antigens.

IMMUNODEFICIENCY

The alterations in immune system, which decrease the effectiveness or destroy the capabilities of the system to respond to various antigens are designated as immunodeficiency. This precarious situation may be attributed to poorly developed immunocompetence or depressed immunity as a result of genetic and environmental factors. Immunodeficiencies are thus classified as congenital or primary and acquired or secondary.

Congenital immunodeficiency

In this type of immunodeficiency, the defect in immunity is genetically determined and is present in animals since their birth due to defect in basic cellular components *e.g.* stem cells, defective genes, defect in enzymes and/or defective expression of cell components. This is characterized by combined immunodeficiency syndrome (CIS), defects in T-lymphocytes, defects in B-lymphocytes, partial T- and B-cell defects, deficiency of complement, and defects in phagocytosis.

Acquired or secondary immunodeficiency

An animal can acquire the suppression of immune system due to drugs, diseases, deficiency of nutrition, neoplasm or environmental pollution which is clinically manifested by increased susceptibility to infections, vaccination failures, recurrent infections and occurrence of new diseases and neoplasms. Most of the pesticides studied during last two decades are found to exert immunosuppressive effect on both the wings of immune system *i.e.* humoral and CMI. Organochlorines, organophosphates, carbamates and synthetic pyrethroid pesticides were found immunotoxic at "no adverse effect dose" levels in poultry, sheep, and in bovine calves. However, the organochlorines are comparatively much more harmful to immune system. They are considered to be the cause of vaccinal failures or occurrence of disease epidemics in animals due to lowered immunocompetence. It has also been reported that a state of immunosuppression for a longer period may also lead to the development of neoplasms as the immune surveillance mechanism becomes defective. Such animals also exhibit recurrent bacterial infections due to defective phagocytic machinery of the body. Immunosuppressive state of animal for a longer duration may also lead to development of cancers in the absence or defective immune surveillance in body. Since the pesticides affect specific as well as paraspecific immune system adversely, the immunosurveillance in body becomes defective. Though, there is no direct correlation but for an example, there is an increased incidence of eye cancer (squamous cell carcinoma of eye) in cattle and buffaloes in western UP during last few years. Similarly the occurrence of canine venereal tumours also increased in dogs during last decade. It is an indication of the adverse effects of polluted environment and may be related with a state of immunosuppression.

Nutritional factors and immunomodulation

To reduce the immunodeficiency, there are some of the nutrients which are necessary for the body system. These may be minerals (trace materials), vitamins, roughages, antioxidants, lipids, Carbohydrates, Proteins, Ionophores, Carotenoids, Bioflavonoids, Omega-3 fatty acids, etc. All these are necessary for the development of the body to improve the nonspecific and specific immunity.

| | Nutrients | Immunomodulation |
|----|---|---|
| 1. | Boron (Fruits and vegetables, cabbage and grains) | Enhance Brain Function, Immunopotentiality |
| 2. | Calcium (Soybean, peanut, sardine, sunflower) | Helps to maintain proper nerve and muscular function, |

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| | seeds, dried beans, grains and unrefined cereals) | protecting immune system |
| 3. | Chromium (Molasses, whole grains) | Increase <i>in vitro</i> lymphocyte proliferative responses to ConA |
| 4. | Cobalt (Vitamin B-12 supplements) | It helps to form the red blood cells, maintain nerve tissues, protecting immune system. |
| 5. | Copper (Molasses, nuts, seeds) | Protection of the tissues against free radicals. |
| 6. | Iodine (Sea foods, seaweeds like kelp) | Influences the nutrient metabolism, nerve and muscle functions, protecting immune system. |
| 7. | Germanium (Garlic, mushrooms, onion, aloe vera, comfrey, ginseng) | Saves the body from harmful toxins and poisons, reducing damage from radioactivity, protecting immune system. |
| 8. | Magnesium | Key substance for proper functioning of the nervous system. Enhance natural killer cell and macrophage activity. |
| 9. | Molybdenum | Key for growth and development of the nervous system, prevent against mental disturbance. |
| 10. | Phosphorous | Key component of DNA and RNA, contribute to tissue growth and repair, nerve impulse, central nervous system health. |
| 11. | Potassium (Whole grains, nuts, dairy products) | Required for protein synthesis and flow oxygen to the brain. |
| 12. | Selenium (Whole grains, asparagus, garlic, eggs, mushrooms, sea food) | Protecting cells and tissues from free radicals. Increases natural killer cells and cancer fighting cells. |
| 13. | Sodium (Salt) | Together with potassium and chloride sodium maintains fluid distribution and pH balance, control; muscle contraction and nerve function. |
| 14. | Sulfur (Peas and beans) | Helps the body to resist bacteria, and protects the protoplasm of the cells, slows down the disintegration of the tissues and cells and slows the aging process. |
| 15. | Zinc | Integral part in the synthesis of DNA and RNA, the genetic material that control cells growth, division and function, immune function. |
| 16. | Copper | Increase the activity of phagocytic cells. |
| 17. | Iron (Green vegetables) | Immune system keeps invading microbes in check by depriving them of iron via a specific immune defense substance called lactoferrin. |
| 18. | Vitamin A (Carrot) | Enhances white blood cell function, enhances resistance to infection and carcinogens. |
| 19. | Vitamin E (cabbage, cauliflower and in green leaves) | It helps to protect vitamin A and red blood cells. |
| 20. | Vitamin B (Externally in the form of B-Complex) | Helps to maintain the healthy skin and well functioning of the nervous system. Immune cell growth and division. |
| 21. | Vitamin C (Fruits and vegetables) | Increases the production of infection fighting white blood cells and antibodies, interferon. Preventing the entry of virus. |
| 22. | Immunoglobulins (IgG) Produced by the B- lymphocytes | It has the capacity to quickly bind with foreign substances leading to opsonization. |
| 23. | Immunoglobulins (IgM) Produced in body during primary immune response. | Neutralize antigen agglutination. |
| 24. | Immunoglobulins (IgA) IgA produced in body surfaces is either secreted on surface through epithelial cells or diffuse in blood stream. | Neutralize the antigen and agglutinate the particulate antigen. Prevents adherence of foreign particles/ antigen on the body surfaces and it can also act inside the cells. |
| 25. | Immunoglobulins (IgE) Very low concentration in serum. | It mediates hypersensitivity type I reaction and is responsible to provide resistance against invading parasitic worms. |
| 26. | Carotenoids (Daily fibrous food) | Increases the number of fighting cells, natural killer cells, and helper T- cells, mops up excess free radicals that accelerating aging, protects against cancer, by stimulating the macrophages to produce tumor necrosis factor. |
| 27. | Bioflavanoids (A wide variety of fruit and vegetables) | Aids the immune system by protecting the cells of the body against environmental pollutants, toxins or germ. |
| 28. | Omega-3-fatty acids (Cod liver oil) | Increasing the activity of phagocytes, the white blood cells, protect the body against damage from over reactions to infection, |
| 29. | Arginine | The amino acid l-arginine augments T-cell response and may be helpful in hastening surgical recovery. |

An adequate supply of good quality of protein containing essential amino acids, certain vitamins, minerals, and trace elements are must to ensure protection of body and health against infectious diseases through successful operation of the immune mechanism. Demands for these nutrients are greatly increased during the production of immunity following diseases/vaccinations. The nutrient discussed the best guidelines during a generalized immune response. Clearly, then, the way is open to a better understanding of how synergistic application of vitamins, minerals, proteins and other nutrients and plant-derived factors can optimize immune function.

Microbial products and Immunomodulation

Crude preparations of some microorganisms are also used as immunomodulator which enhances the both specific and paraspecific immunity in animals and man. The Freund's complete adjuvant derived from *Mycobacterium phlei* is used in nonspecific manner. *Corynebacterium parvum* now classified as *Propionibacterium acnes* has been associated with immunostimulatory activity in man and domestic animals. The *Propionibacterium acnes* is effective in increasing immunity against bacterial, viral and protozoan infections. It activates the macrophages, increases antibody synthesis, increases T-cell responsiveness and induces cytolytic responses of T-cells against tumor cells. Lentinan, a neutral polysaccharide derived from fungus *Lentinus edodes* is also found to have immunomodulatory property. It was found to stimulate pinocytosis of murine peritoneal macrophages, to increase the production of interferons, to enhance the production of interleukin-1. It enhances both specific as well as paraspecific immunity in animals.

Synthetic chemical compounds and Immunomodulation

| Synthetic chemical compounds with immunomodulatory properties | | |
|---|---------------------|--|
| 1. | Levamisole | Increase T-cell and macrophage activity |
| 2. | Thiabendazole | Enhances lymphocyte blastogenic responsiveness to mitogens |
| 3. | Imuthiol | Increases lymphocyte blastogenesis, IL-2 production |
| 4. | Avridine | Increases bactericidal activity of neutrophils |
| 5. | Isoprinosine | Increases T-helper cells |
| 6. | Glucan | Enhances chemotaxis for neutrophils |
| 7. | Indomethacin | Increases blastogenic responses of T-cells |
| 8. | Ascorbic acid | T-lymphocyte proliferation, lymphokine production, increases Ab production |
| 9. | Bioestim | Improves DTH reaction |
| 10. | Dihydrohepataprenol | Increases number of neutrophils |

In this group, mainly 3 chemical compounds are extensively studied including levamisole, synthetic polynucleotides and isoprinosine. Levamisole was originally developed as an anthelmintic for man and animals. But apart from its anthelmintic activity, it was also found to exert immunopotentiating effect. From the extensive studies, it has been observed that levamisole is having a marked effect on cellular immunity with little effect on antibody production. Also, it is effective only when the animal's immune system is functioning sub optimally.

Isoprinosine is a synthetic immunomodulator which is also having antiviral activity. It enhances lymphocyte proliferative responses, increases lymphokine production and increases NK cell cytotoxicity. Immunosuppression caused due to viruses or cyclophosphamide can be restored by isoprinosine treatment. But this has no effect on B-cell proliferation induced by lipo-polysaccharides.

Synthetic polynucleotides is a complex of high molecular weight and was found to augment natural killer cell activity, activate macrophage tumoricidal activity, stimulate lymphocytes to PHA and enhance delayed type hypersensitivity responses to sheep red blood cells. Polynucleotides have dual effect on antibody production; if antigen is administered within hours of polynucleotide administration, helper cells tend to dominate the response, whereas if antigen administration is delayed to 24 hrs it leads to immunosuppression. The inherent toxicity of polynucleotides tends to limit their usefulness as therapeutic immunomodulators in animals. The toxic effects of polynucleotides include pulmonary thrombosis, hepatic neurosis, reduced body weight, elevated blood urea nitrogen and leucopenia.

Herbal immunomodulation

In Ayurveda, the life describes four types of therapeutic approaches namely Prakrati Sthapanam (maintenance of health), Roganashani chikitsa (cure of disease), Naishtiki chikitsa (spiritual therapy) and Rasayana chikitsa (herbal product therapy). The rasayana therapy is useful for preventing the diseases. The rasayana drugs are endowed with multiple properties like delaying ageing, improving mental functions and preventing diseases.

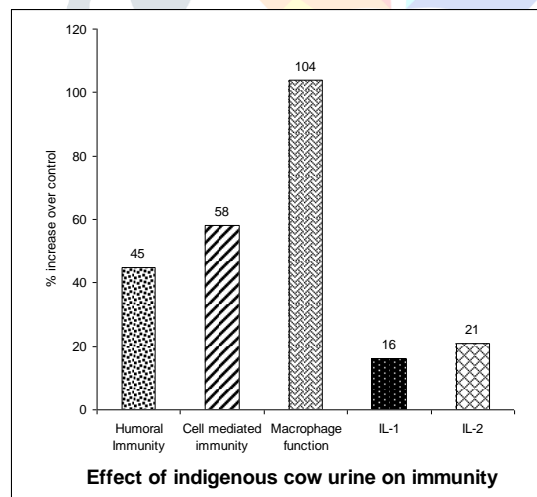
Plants having immunomodulatory properties

1. Giloy (*Tinospora cordifolia*)
2. Ashwagandha (*Withania somnifera*)
3. Aonla (*Embllica officinalis*)
4. Pipali (*Piper longum*)
5. Tulsi (*Ocimum sanctum*)
6. Neem (*Azadirachta indica*)
7. Bach (*Acorus calamus*)
8. Safed musli (*Asparagus adscendens*)
9. Arjun (*Terminalia arjuna*)
10. Makoy (*Solanum nigrum*)
11. Mushroom (*Agaricus sp.*)
12. Chhota Gokhru (*Xanthium strumarium*)
13. Clove (*Syzygium aromaticum*)
14. Safeda (*Populus alba*)
15. Jar-Amla (*Phyllanthus niruci*)
16. Kirayat (*Andrgraphis paniculata*)
17. Turmeric (*Curcuma longa*)
18. Saunf (*Foeniculum vulgare*)
19. Kasni (*Cichorium intybus*)
20. Kali Haldi (*Curcuma zedoaria*)

There are many herbs which are known to exert their immunomodulatory properties, of which some of them are studied scientifically but most of them are yet to be scientifically validated. *Tinospora cordifolia*, *Withania somnifera*, *Asparagus racemosus*, *Embllica officinalis*, *Piper longum*, *Terminalia chebula*, *Borrhevia diffusa* and *Acorus calamus* are found to be immunostimulant in different models of immunosuppression or infections. *Tinospora cordifolia* prevented cyclophosphamide induced immuno-suppression as well as immune response in suppressed mice. These herbs exhibited an array of diverse biological activities such as antistress, adaptogenic, anti ageing and immunomodulatory activity.

The extract of *Azadirachta indica* (neem) is found to stimulate the phagocytic activity and antigen presenting ability of macrophages and enhances the mitogenic response of spleenocytes to ConA. Besides, it is also effective against allergic disorders and desensitizes the host to specific allergens limiting the danger of anaphylactic reactions. The *Piper longum* (pipali) is found to be effective in prevention and control of giardiasis in human beings.

Cowpathy and Immunomodulation



Cowpathy is just like any other system of medicine such as Homeopathy, Allopathy or Naturopathy. In this, the human or animal ailments are treated with products of cow also known as Panchgavya means five things derived from cows i.e. milk, ghee, dahi, urine and dung. In our ancient literature of Ayurveda it is described as Panchgavya Chikitsa. In recent years, interest has been generated among scientific community of the world to develop or scientifically validate the Indigenous Technical Knowledge (ITK) as an alternate therapeutic or preventive approach. As is evident from the trends of modern allopathic treatments particularly the development of resistance in microorganisms and side effects, the alternative system of medicine gains momentum not only in India but WHO also established recognition to such systems. In fact in the western world also, scientists/ clinicians are facing problem in handling the multiple drug resistance in microorganisms, presence of antibiotic residues in food chain and/or associated allergies and autoimmune disorders in man. As per WHO, the twentieth century wonder drugs "antibiotics" will not remain useful and become almost ineffective by the year 2020, then one has to think over the alternative therapeutic approaches to control the infections. In fact most of the antibiotic drugs are bacteriostatic in nature and as such they do not kill the bacteria rather they stop or check their growth and bacteria have to be destroyed by the body's own defense

mechanism known as “Phagocytic System” through macrophages (monocytes of the blood). During last few years it has been observed that the efficiency of these macrophages reduced drastically as a result of the environmental pollution and presence of pesticides, heavy metals, fungal toxins etc. in the food chain. That is attributed to the heavy use of agrochemicals in agriculture and poor storage conditions of food grains. Anyhow deficient functioning of macrophages leads to inefficacy of antibiotic drugs, development of resistance in bacteria, recurrent infections, and or decreased immune status of an individual. Recent researches showed that cow urine enhances the immune status of an individual through activating the macrophages and augmenting their engulfment power as well as bactericidal activity. This research opened a new era in medical science and CSIR has got a patent from US on cow urine for its bio-enhancing properties and its use in tuberculous patients. Along with traditional therapy of tuberculous drugs, if one also consumes cow urine, the anti-tuberculous drugs act faster even in low doses and thereby reducing the cost of treatment and its duration. Recently, research have found that use of cow urine along with the antibiotics prevents the development of resistance in microorganisms against the antibiotics. This is thought that the cow urine blocks the R-factor, a part of plasmid genome of bacteria responsible for the development of antibacterial resistance. Several scientists from different laboratories of CSIR, AIIMS, G.B. Pant University Pantnagar, and IVRI, besides NGOs are working on different medicinal properties of cow urine. In fact there are several medicinal preparations available with NGOs who are also marketing cowpathy drugs under FDA license and some of the NGOs are even not able to cope up with the demand of the public. Several students of M.Sc., M.V.Sc., M.D. and/or Ph.D. are working on the medicinal properties of cow urine and other products of cows. It has been found to enhance the body's immunity and resistance power to fight with infections. Cow urine has antioxidant properties and thus it neutralizes the oxidative stress produced in body through action on free radicals. It has been found to repair the damaged DNA and thus is effective for the cancer therapy. Scientists proved that the pesticides even at very low doses cause apoptosis (cell suicide) in lymphocytes of blood and tissues through fragmentation of DNA and cow urine helps the lymphocytes to survive and not to commit suicide, it also repairs the damaged DNA. Besides, in poultry cow urine enhances the immunocompetence of birds and provides better protection along with vaccination. It also increases egg production, egg shell quality and egg weight. Moreover, by using cow urine in poultry ration one can enhance the productivity that too without using antibiotics and the fear of antibiotic residues in poultry products.

On the basis of chemical fingerprinting through modern equipments like HPLC, it has also been observed during the scientific research that the urine of Indian cows are highly effective and almost nil or few medicinal properties are present in the urine of crossbred, exotic cows, buffaloes, etc. The Indigenous cow urine contains “Rasayan” tatva, which is responsible to modulate immune system and act as bioenhancer. It is not only the cow urine which is a wonder product by cow but others like dung, milk, ghee and curd are also equally effective for various ailments and other operations. Similarly, many medicines are prepared from the cow milk, ghee and curd. However, again the problem is same, scientific validation of these products is required on regular basis in order to have confidence in the stake holders.

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