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A Study on Anti-Arthritic Activity of Plants

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Nature and evolution have provided all the organisms, from lower invertebrates to the higher organisms with a vigilant defence against any pathogenic attack or injury faced in day to day life. In recent years, several literatures have revealed that some orders of plants also possess certain degree of defense mechanism against the pathogen invasion or injury. Survival of any living organism is nearly impossible without this vigilant defense system which is well-known as the immune system (Tracey JK, 2002). Immune system helps in maintaining homeostasis by exploiting a dynamic network which involves the use of large number of cells and molecules capable of recognizing and distinguishing the foreign invaders from the self-cells.

Immune system works by utilizing two distinct units of immunity named as innate and adaptive immunity. Innate immunity acts as the first line of defense. It involves the role of cellular and molecular mechanisms which are ready to act in immediate manner in case of any infection or foreign invasion (Turvey and Broide, 2010). Innate immune system works by exploiting the physical, chemical and cellular barrier.

Physical barrier involves the skin as well as the mucous membrane in the body. Chemical barrier involves the chemicals like acidic secretion of the stomach, lysozyme secreted by the tear glands etc. Cellular barrier involves a group of cells like neutrophil, macrophages etc. which are capable of distinguishing foreign cells from self-cells, but they do not possess the ability to detect the small differences between the foreign cells (Kuby, 6th edition). If the pathogen or any foreign cell is able to evade the first line of defense i.e. the innate immunity, then the immune system cells into play the second line of defense mechanism known as the adaptive immunity (Schmid and Munz, 2007). Adaptive immunity works by utilizing the B- cells and Tcells.

These are capable of recognizing and effectively eliminating the foreign invaders or altered self-cells. After identification and elimination of pathogen or non self-cells, they develop immunologic memory. Immunologic memory helps in developing increased immune response towards the pathogen in case of second or subsequent encounter by the body thus providing lifelong immunity (Kuby 6th edition; Paul WE, 5th edition).

Immune system, of our body is working under strict surveillance for protecting against any kind of infection or disease due to any exogenous factors like microbes etc. or any endogenous factors like altered or defective self-cells. But sometimes immune system fails to provide adequate protection to the host organism. In some cases the immune system does not respond adequately to the foreign invasion leading to the case of immune-deficiency and development of diseases as AIDS, cancer etc.

Whereas, in some cases, the immune system becomes hyperactive and starts recognizing self-cells as non-self thus leading to development of auto-immune diseases like diabetes mellitus, rheumatoid arthritis etc. (Medzitov R, 2008).

Since ages, in case of any immunodeficiency or hypersensitivity due to the failure of immune system, humans have switched over to the use of various other means like immune modulation in order to restore the normal functioning of the immune system.

Immuno-modulation is a phenomenon of altering the immune function by either suppressing the immune response (immuno-suppression) or augmenting the immune response (immuno-stimulation/ immuno-potentiation) through the use of organic chemicals of synthetic or natural origin commonly referred to as immunemodulators.

Of the various immune-modulators available, natural products obtained from plants (phytochemicals) have been a major area of interest. Since ages plants have been heavily exploited by the humanity for the treatment of various infection and diseases.

Role of Phytochemicals in Immuno-modulation Exploitation of whole plant or its various parts for the treatment of disease comes under the ancient branch of science known as Ayurveda. Further, the use of knowledge provided in ayurveda as well as in folklore tradition for scientific research regarding the role of plants in treating various diseases is termed as Ethano pharmacology. Ayurveda has played a major

role in life of humans since ancient vedic civilization of India. The origin of ayurveda and the use of medicinal plants in various disease dates back somewhere between 2500- 500 BC (Samy PR, et al., 2008). The sanskrit term ayurveda comes from two different words “ayus” meaning life and “veda” meaning knowledge. Hence, ayurveda is “science of life” focussing on man and cure of his illness using the knowledge of medicinal plants (Micozzi MS, 2nd Edition). Using various parts of the plant as well as plant products (phytochemicals), ayurveda works on the principle of maintaining a balance in immune system through the process of immuno-modulation (Oberholzer A, et al., 2000). Hence, since vedic times, plants and its phytochemicals are looked upon as potent immuno-modulators, playing a significant role through immune suppression or immuno- potentiation.

Plants are a rich source of various metabolites. They contain two categories of metabolites named as primary metabolites and secondary metabolites. Primary metabolites includes those substances which contribute a major role in plant structure as well as energy metabolism of the plants. These basically include the carbohydrates, proteins and fats. Secondary metabolites are the group of chemicals not required by the plant for its structure or function and are comparatively found in less quantity as compared to the primary metabolites. These are a group of non-nutritive dietary components, some of which are utilized by plants in defense system. The compounds which fall under the category of secondary metabolites are broadly categorized as “phytochemicals” (Leitzmann C, 2nd edition). Phytochemicals, are the defense molecules present in the plant to protect from various microbes, insects etc. They also act as growth regulators in the plant system.

Secondary plant metabolites or phytochemicals possess pharmacological properties which was scientifically for the first time was mentioned by AG Winter (Winter, 1959). Since then various scientific studies are being carried out to study the therapeutic potential of various plants and their products. Till date many plants have been shown to possess significant immuno-modulatory role thus proving to be a potential tool in drug discovery and drug development Inflammation

The word inflammation has been derived from a latin word “inflammare” which means “to set on fire”. Roman scientist Cornelius Celsus in 1st century AD described inflammation and its four cardinal signs stating “rubor et tumor cum calore et dolore” meaning that redness and swelling accompanied with heat and pain. Another scientist who contributed in the early era to this field of inflammation was John Hunter who in 1973, put forward to the fact that inflammation is a process which is actively working in host defense rather than as a disease process which was actually presumed (Paul WE, 4th Edition).

The moment any invading pathogen, harmful chemical or tissue injury is encountered, a complex cascade of events occurs inside our body which involves the action of inflammatory cells, and is termed as inflammatory response and the whole process is known as inflammation. It is one of the initial response taken up by our innate immune system. In the physiological condition that is generated during the process the inflammatory process, it protects our body against any further tissue injury as well as help in clearing the damaged tissue. Further, in case of any pathologic condition, the inflammatory condition can lead to tissue destruction and organ dysfunction.

Therefore, controlled inflammatory process is very necessary. The inflammatory condition can also turn detrimental if the process of inflammation is dysregulated as reported in pathological inflammatory state which is assumed to be a counterpart of physiological condition (Medzhitov, R, 2008). Because of the dual characteristics of inflammation i.e. being beneficial as well as detrimental, it is sometimes also referred to as the “double edged sword” (Paul WE, 5thEdition).

Various cells are also known to play key roles in initiation of inflammation such as neutrophil, NK cells, macrophages and dendritic cells. The response generated during acute inflammation after any tissue injury or pathogen invasion is generally unbiased and initiated in the similar manner. Within minutes after any kind of tissue injury there is an increase in the vascular diameter of the blood vessels resulting into the increase of blood flow. The rise in the blood volume at the affected area leads to the heating of tissue thus increasing the redness. Further, it also leads to the increase in the vascular permeability of blood vessels especially at the post capillary venules thus resulting into the leakage and accumulation of fluids from blood vessels at the site of tissue injury forming a condition of edema (Kuby, 6th edition). After few hours of tissue injury, the leukocytes adhere to the walls of endothelial cells and through the process extravasation and rolling mechanism in the capillaries they migrate to the site of inflammatory stimulus. These leukocytes are the first inflammatory cells to respond to any kind of inflammatory stimulus. Leukocytes initiate the inflammatory process through phagocytosis of invading foreign particles.

During this process, these cells trigger the release of various inflammatory mediators which contributes to the inflammatory response and recruitment of other effector cells, playing significant role during inflammation (Basset C, et al., 2003).

Sometimes, due to membrane permeabelization and perturbrations some of the lipid molecules on the membrane of inflammatory cells like macrophages, neutrophil, mast cells etc. gets degraded thus resulting into the production of arachidonic acid and

lyso platelet activating factors, which further leads to the increased condition of inflammation.

From all the above mechanisms, it is very clear that as soon as any tissue injury or septic shock occurs to any part of the body or any foreign particles tries to invade our body, the acute inflammatory response immediately comes into action in order to restore the homeostasis. As soon as the foreign threat is eliminated from the body, the inflammatory condition subsides down due to the activity of various anti-inflammatory mediators. But in certain immune-deficient or auto-immune disease where the inflammatory condition persists for a longer duration, it leads to an advance stage of inflammation known as "chronic inflammation".

ROLE OF MACROPHAGES IN ARTHRITIS

Macrophages are one of the key players in most of the chronic inflammatory diseases (Allison and Davies, 2004) like arthritis and act as an important link in development of chronic inflammation through persistence of acute inflammation. In normal joints the synovial lining is a very thin layer which consists of very less number of macrophages and fibroblast cells which are present in inactive form. During arthritis the synovial lining increases in thickness which mainly occurs due to proliferation of synovial fibroblast along with the increased infiltration of large number of lymphocytes and macrophages (Yingyu and Pope, 2005).

These macrophages play an active and major role in development and progression of arthritis by promoting inflammation and joint destruction in arthritis. These cells accumulate at the synovial linning as well as at the junctions of cartilage and pannus (Mulherin D, 1996). These cells release a high amount of inflammatory cytokines and chemokines like IL-1H, TNF-G, IL-6, IL-8, MCP-1 etc (Kinne RW, et al., 2000).

Further, it results in bone destruction and enhanced recruitment of osteoclast precursors which differentiate into mature osteoclast cells (Yingyu and Pope, 2005). Macrophages are one of the interesting targets for treating arthritis as the infiltration of synovial macrophages are associated with the degree of radiological progression via bone destruction. It is also reported that the conventional anti-rheumatic drugs work through the down regulation of mononuclear phagocyte system. Besides all, the biological therapies available for treating arthritis also aim at down regulating the cytokines which are released via macrophages (Kinne RW, et al., 2000).

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