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Review Article

# Inflammatory Process and Role of Cytokines in Inflammation: An Overview

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**Abstract** | Inflammation is the first line of defense in invertebrates and vertebrates as it helps in fight against tissues injury or foreign invaders. Uncontrolled or excessive inflammation is destructive for normal homeostatic processes of body. Most of the modern human diseases such as asthma, allergy, autoimmune diseases, hepatitis, coeliac disease, inflammatory bowel disease and glomerulonephritis are linked directly or indirectly to different inflammatory processes. Conventionally, different steroidal and non steroidal drugs i.e., antibiotics are used to treat inflammatory disorders. Theses synthetic drugs have many side effects on the health such as gastrointestinal problems, stomach ulcers, dizziness, liver or kidney problems etc. Cytokines play an important role in the induction and suppression of inflammation. Cytokines are diverse form of proteins that act pro- and anti-inflammatory cytokines. The main component of immunity is IL-1. IL-6 cytokine play its role in regulation of metabolic reactions. The activity of various leukocytes is suppressed by IL-4 and IL-10 (anti-inflammatory cytokines) that triggers the production of pro-inflammatory cytokines. This review paper provides an overview of inflammation, its associated factors, causes and treatment and role of cytokines in inflammation.

**Novelty Statement** | This review article provides an overview of sericulture activities in Pakistan and different food supplements to enhance the biological and economic traits of silkworms.

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## Introduction

Word inflammation was originally derived from the Latin word inflammare (Basra *et al*., 2019) which means burned (Joseph and George, 2016; Actor and Smith, 2019). The main part of body's protective mechanism is inflammation (Greten and Grivennikov, 2019). It is a process through which lymph node recognizes the infectious pathogens, cell damage (Mohod *et al*., 2016), local injury and toxins (Takeuchi and Akira, 2010; Medzhitov, 2010). It eliminates harmful stimuli and starts the healing phenomenon. Inflammation is a biological response that disturbed tissue homeostasis. Various aging-related ailments and certain cardiovascular disorders are associated with inflammation (Libby, 2007).

*Signs of inflammation*

The indications of inflammation are well-known to mankind for hundreds of years i.e. pain (dolor) (Mohod *et al*., 2016), warmth or heat (calor or hyperthemia) (Libby, 2007), swelling of tissues (tumor) (Lawrence *et*

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*al.*, 2002) and redness (rubor) (Lajili *et al.*, 2016). These symptoms were documented first time in the history in 1st century AD by Roman encyclopedist, Aulus Cornelius Celsus (Xiao, 2017). Another important symbol of inflammation is failure of the function of the infected part, which was added by Rudolph (1858) in his book Cellular pathologie (Korniluk *et al.*, 2017; Missiroli *et al.*, 2020). Remarkably, the earlier four cardinal symptoms apply merely to acute inflammation. Functio laesa (loss of function) is predominantly the symptom associated with all inflammatory processes.

*Types of inflammation*

Inflammation can be of two types i.e. acute or chronic (Fritsch and Abreu, 2019). It is an extremely conserved process and seems to be a significant first line of defense for both vertebrates (Abarike *et al.*, 2019; Sharrock and Sun, 2020) and invertebrates (Sharrock and Sun, 2020). Acute inflammation is a short term (may occur from seconds to days) and early response in the host body produced by innate immunity. Countless cells are produced by innate system that play its vital role in inflammatory response (Waisman *et al.*, 2015). Unlike adaptive immunity, innate immune system does not have capacity to differentiate between various strains of disease causing agents. It may cause edema and increased blood flow, migration of neutrophils at site of inflammation and movement of fluid from capillaries to interstitial fluid (Waisman *et al.*, 2015). It heals the injured tissues and also fights with the foreign invaders (Majno and Joris, 2004).

Chronic inflammation is recognized as an adaptive response that possesses (holds) prevalent and extensive nature affecting cellular homeostasis and the normal functioning (Drayton *et al.*, 2006). It confronts more harmful effects on host, if it continues longer such as during cancer (Grivennikov *et al.*, 2010), heart attack (Medzhitov, 2010) and Alzheimer's disease. Chronic inflammation is characterized by the invasion within the primary inflammatory cells including plasma cells, lymphocytes and Macrophages secreting inflammatory cytokines, development factors and proteins (Cutolo *et al.*, 2019). They cause tissue deformation and repairment including granuloma formation and fibrosis etc. (Cutolo *et al.*, 2019) (Figure 1).

*Process of inflammation*

In response to any harmful or foreign molecule, inflammation generally starts within few minutes by indentation of immune system (Artis and Spits, 2015). Innate system comprises immune cells that include lymphocytes, dendritic cells (DC's), neutrophils, macrophages and mast cells that play significant functions in inflammatory reactions. Firstly, the pathogens get adhere to particular receptors i.e. G-protein attached receptors (Sun and Richard, 2012), Pattern realization receptors (Takeuchi and Akira, 2010) and Chemokine receptors (Charo and Ransohoff, 2006). The fabrication of the inflammatory cytokines including IL-1, IL-6, chemokines and TNF is initiated by these receptors. These inducers quickly change the vascular endothelial permissibility and releases antibodies, complement factors and neutrophils in the site of septicity (Snapper and Abraham, 2013).

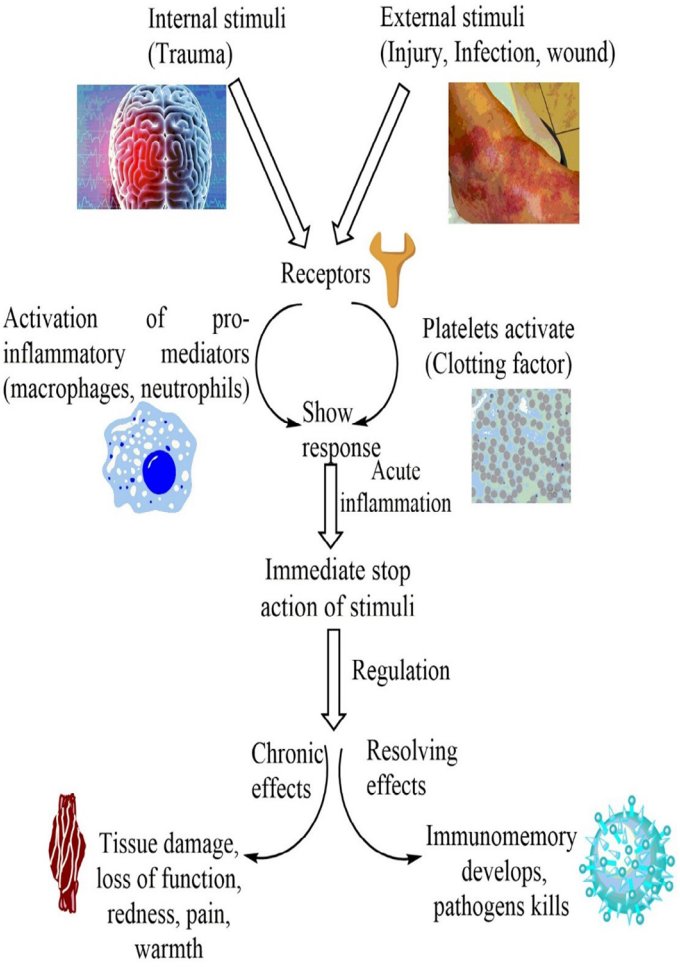


**Figure 1: Acute and chronic Inflammation in mammals.**

The inflammatory cytokines increases the excretion of coagulation factors and C-reactive protein by means of the liver cell. They invoke brain endothelium and smooth the secretion of prostaglandins (Jarapula *et al.*, 2016). They are important for the key symptoms of pain and fever via their detrimental effects on CNS (central nervous system) (Medzhitov, 2010) (Figure 2). Alternatively the viral contamination follows one kind of signaling pathway via producing different type of cytokines known as type-1 interferons (IFN's). Furthermore, parasitic infections and allergens invoke the assembly of other inflammatory cytokines IL-13, IL-5, and histamine where the rest of the pathway is nearly the same (Medzhitov, 2010; Rose-Johnston, 2017).

*Mechanism of inflammation*

Inflammation is a complex biochemical mechanism which leads to the stimulation of infectious agents

and promotes injury. It causes tissue damage and pain monitored through treatment (Del Giudice and Gangestad, 2018). Chemical agents are secreted by immune cells like cytokines, chemokine and reactive oxygen species at injury site to eliminate pathogens (Diakos *et al*., 2014). A major constituent of inflammatory process is arachidonic acid which is a by product of fast acting cell membrane. Arachidonic acid is transformed into prostaglandins and thromboxane enzyme by cyclooxygenase (COX) (Jayesh *et al*., 2020).

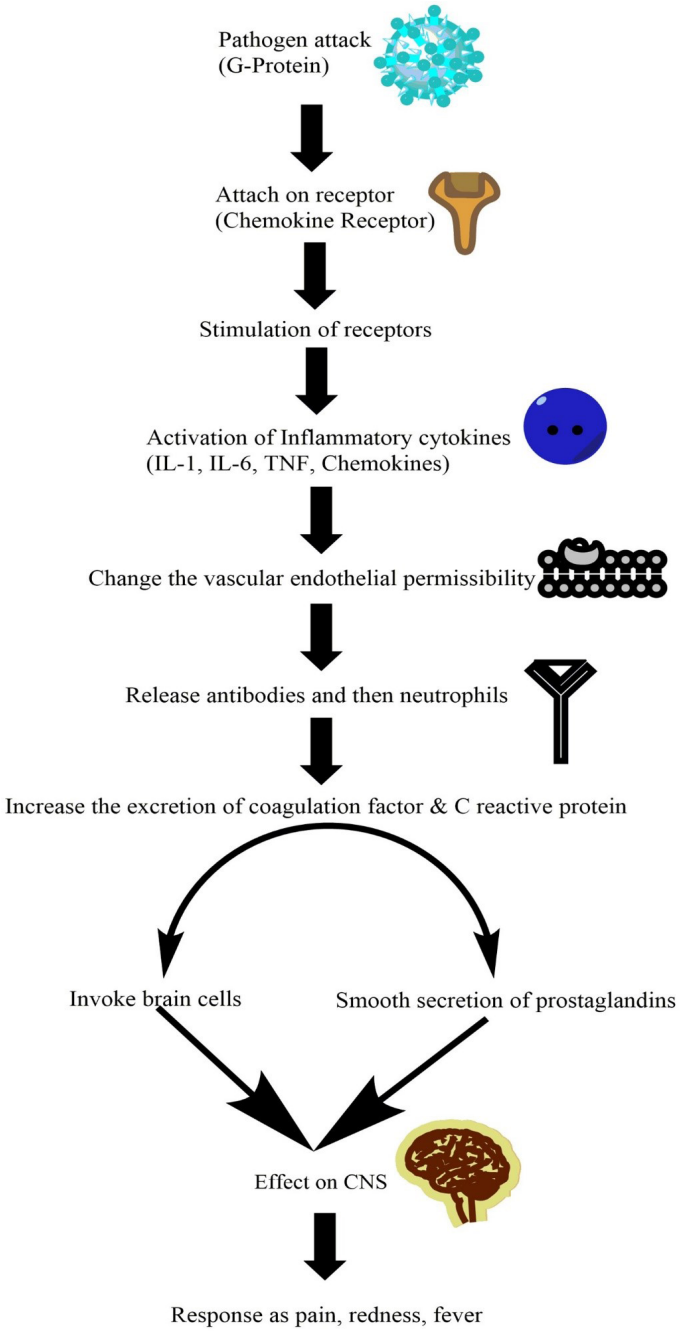


**Figure 2: Steps during inflammatory process.**

Neutrophils begin to attach strongly to the endothelium by using carbohydrate ligands to show symptoms of inflammation. Endothelial cells in their stimulated form are responsible for the production of surface bonded and soluble particles. They produce a strong adhesion between neutrophils and endothelium. Neutrophils leave the bloodstream and travels across endothelium (Merritt, 2019). Production of particular cells like cell adhesion molecules (CAMs), their activators and chemical stimulus is responsible for the neutrophils emigration (Yoshizaki *et al*., 2010). Molecular or cellular actions of infectious response tend to increase blood movement, capillary damage, leukocytes access and the creation of chemical agents (Valacchi *et al*., 2018). Stimulation of these chemical agents initiates the formation of inflammatory cytokines including TNF, IL-1, chemokines and IL-6 that causes tissue damage. Due to phagocytic activity of cells, migratory neutrophils are eventually removed from inflammatory site through apoptosis and produce anti-inflammatory cytokines (Ansar and Ghosh, 2016; Brod, 2017) (Figure 3).

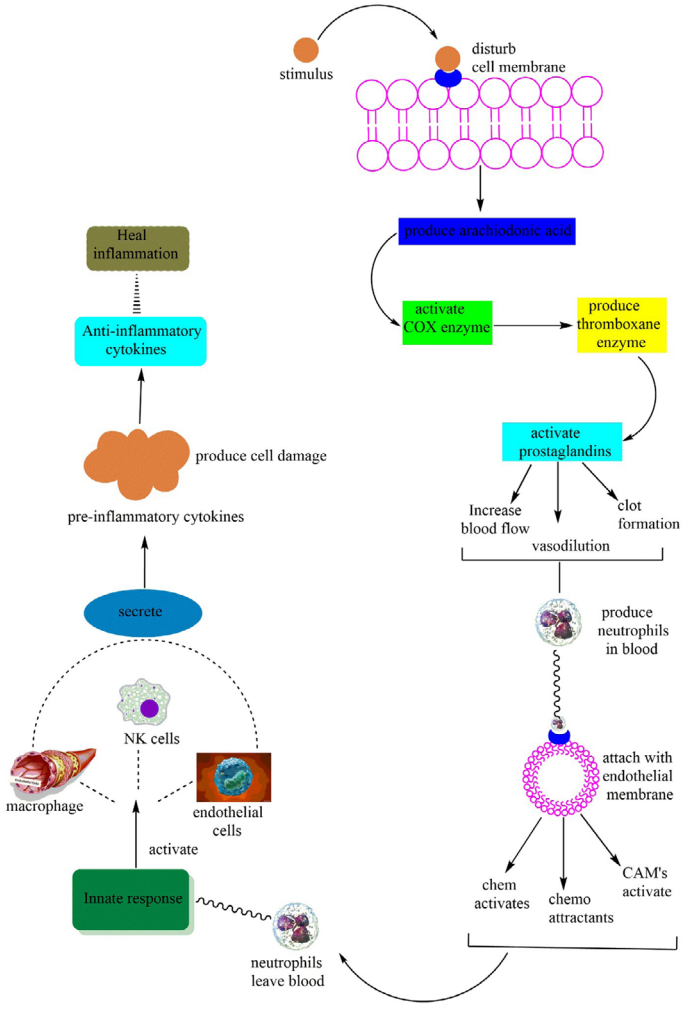


**Figure 3: Mechanism of inflammation.**

*Treatment of inflammation*

Inflammation can be cured by using anti-histaminic, corticosteroidal (Akhtar and Shabbir, 2019), diuretics (Uroos *et al*., 2017) and NSAID's (non-steroidal anti-inflammatory drugs) such as aspirin (Satani *et al*., 2019), ketoprofen, diclofenac (Gupta *et al*., 2019), clinoril, naproxen (Haley and Recum, 2019), sodium salicylates (Duron *et al*., 2020), ibuprofen (Rifai *et al*., 2019),

indomethacin (Munjal and Allam, 2020). These drugs are effective in their action because they reduce inflammation and pain (Joseph and Raj, 2012; Pahwa and Jialal, 2019; Parolini, 2020). They are different in their structural form *yet all* drugs have similar antipyretic, analgesic and anti-inflammatory properties (Sullivan and Farrar, 2011; Abbate *et al.*, 2016; Lundgren *et al.*, 2017).

NSAIDs mitigate pain by lowering neighboring inflammatory reactions by the suppression of prostaglandin synthesis (Lucas, 2016). Corticosteroids and statins are likewise used to decrease inflammation (Pahwa and Jialal, 2019). Dyslipidemia and low-grade inflammation is treated by using metformin. It diminishes circulating IL-1beta, TNF-alpha, fibrinogen and hsCRP (High sensitivity C-reactive protein) (Pahwa and Jialal, 2019). Indomethacin appeared as one of the most highly intense pain relieving and anti-inflammatory medicine through non-particular prohibition of COX (cyclo-oxygenase) enzyme which answerable for the conversion of arachidonic acid into prostaglandins (Abbate *et al.*, 2016; Lucas, 2016). Anti-inflammatory reactions follow after inflammation arrives at its peak and represents to its preventive response (Stankov, 2012).

Indomethacin was first drug among all NSAIDs that was utilized for curing various inflammatory diseases (Mishra *et al.*, 2019; Lopez-Contreras *et al.*, 2020) but was noted to cause disastrous health issues during its long-term use and was considered a hepatotoxic (Abatan *et al.*, 2006), hematotoxic, gastric ulcerogenic (Akpamu *et al.*, 2016) and nephrotoxic agents (Olusegun and Lawal, 2008). Consequently, finding of new and natural medicinal plants and their secondary metabolites with strong anti-inflammatory activity and insignificant detrimental impacts, is demanded (Malathi *et al.*, 2012).

*Diseases caused by NSAID's*

Artificially adapted drugs cause high risk of stroke, kidney problem, heart attack especially uses in higher doses or may cause ulcers, upset stomach or bleeding in intestine or stomach (Tambewagh *et al.*, 2017; Bensman, 2019; Bradley, 2020). It may cause hypersensitivity and symptoms like fever, conjunctivitis, renal failure, dizziness, blurred vision, pancreatitis etc. Nonetheless, there is a limitation on the use of certain medications because of their detrimental effects like ulcer of gastrointestinal tract, renal damage, cardiac abnormalities and bronchospasm (Gosavi *et al.*, 2011; Shah and Alagawadi, 2011; Gupta *et al.*, 2019). Unawareness of the side effects of NSAID's may cause death (Hoxha *et al.*, 2020).

*Natural products and medicinal plants for treatment*

Due to the adverse effects of NSAIDs it is a dire need of hour to move towards natural anti-inflammatory products. New natural medicinal plants and their metabolites with strong anti-inflammatory activity and insignificant detrimental impacts has been exploring by the world scientific community due to its bioavailability and cost efficiency (Malathi *et al.*, 2012). Many plants have been identified which consists of compounds and molecules with anti-inflammatory properties. Their study gained more interest due to their active potential and beneficial effects. These active molecules help the body to defend against inflammatory related pathogens (Tili and Michaille, 2016).

Several natural substances are being used for the treatment of inflammation including bark of yellow willow tree (Klessig *et al.*, 2016), white mulberry, black mulberry, curcumin or turmeric (Patidar *et al.*, 2014; Kocaadam and Sanlier, 2017), ginger, hyssop, resveratrol, quercetin, caffeic acid phenethyl ester, *Harpagophytum procumbens*, piceatannol (PIC), green tea, propolis, cannabis, fibroin and sericin (Pahwa and Jalal, 2019).

The Oryeongsan expressed anti-inflammatory potency by suppressing various mediators of inflammation e.g., IL-6, NO, IL-1β and TNF-$\alpha$. Besides this effect, it remarkably repressed the synthesizes of iNOS and COX-2 enzymes and inhibited the activation of NF-κB signaling pathway (Arulselvan *et al.*, 2016). Edible red algae has porphyran which act as major bioactive compound in this plant. It acts as mediator of anti-inflammation by preventing the activation of NF-κB (Isaka *et al.*, 2015). *Cassia occidentalis* have bioactive compounds i.e. emodin and chrysophanol which help in prohibiting proinflammatory cytokines IL-1β and TNF-α. These compounds have their effective role for the natural treatment and therapy of inflammation (Patel *et al.*, 2014). Sericin influenced the production of few anti-inflammatory cytokines to reduce allergy and skin inflammation (Aramwit *et al.*, 2009). It can suppress the enzyme activity such as COX-2 and iNOS and start healing process. In nature we should prefer these natural products and medicinal plants to reduce any adverse effects of NSAIDs.

*Cytokines*

Cytokines are small sized non-structural proteins. The mass of cytokines ranges from 8000 to 40,000 Da (Gandhi *et al.*, 2016). They are produced by non-immune cells including fibroblast and immune cells includes NKCs (natural killer cells) and T-cells (Taleb *et al.*, 2015). Cytokines have demonstrated the role of inflammation as they are protectors of proteins and have important functions in differentiation for body immune system against pathogens, physiological processes and cell proliferation (Ait-Oufella *et al.*, 2011). To avoid any immune-pathological imbalance, a coordination between various cytokines is required, as the addition of pro-inflammatory cytokines can cause different diseases (Chang *et al.*, 2009).

*Classification of cytokines*

Cytokines are a diversified group of proteins. They are categorized as transforming growth factors (TGF's) interleukins (ILs), interferons (IFN's), colony stimulating factors (CSFs), tumor necrosis factor (TNFs) and numerous chemokines (Chang *et al*., 2009) (Figure 4). The broader classification suggests that the cytokines have two main groups: In first group cytokines are produced from type I (Th1) T helper cells while the cytokines produced from type II (Th2) T helper cells make up the other group. The activation of T lymphocytes and macrophages is the main task of first group while the other group is involved in stimulating humoral responses (Mallat *et al*., 2009). Type 17 T cells and regulatory T-cells are important because of their involvement in inflammation and pathogenesis. Type 17 T-cells regulate the stimulation of myeloid cells in the inflammatory zone (Ait-Oufella *et al*., 2011) and regulatory T cells block the immune response by inhibiting the activation of T-cells (all types) (Mallat *et al*., 2009).

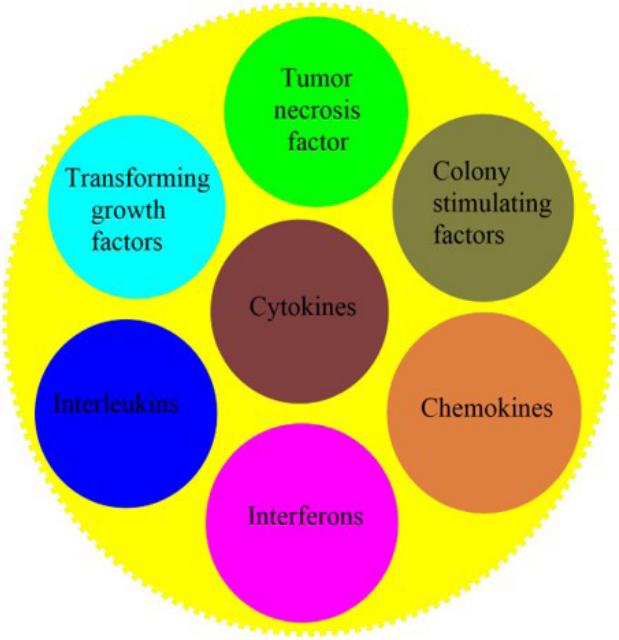


**Figure 4: Classification of cytokines.**

*Types of cytokines*

In inflammation cytokines interact as both pro and anti-inflammatory cytokines (Maspi *et al*., 2016). Proinflammatory cytokines involve gamma interferon, granulocyte M-CSF (macrophage colony stimulating factor), TNF, IL-1, IL-6 and IL-12 (Spangler *et al*., 2015). Anti-inflammatory cytokines i.e. IL-4, IL-10, IFN alpha and IL-13 and transforming growth factor-beta down controls hyperactive inflammatory reactions (Shokryazdan *et al*., 2017) (Figure 5). Instead, by the activation of Th1 cells anti-inflammatory cytokines such as IL-4, IL-10, and IL-13 are produced that can resolve hyper-active inflammatory reaction (Wolde *et al*., 2020).

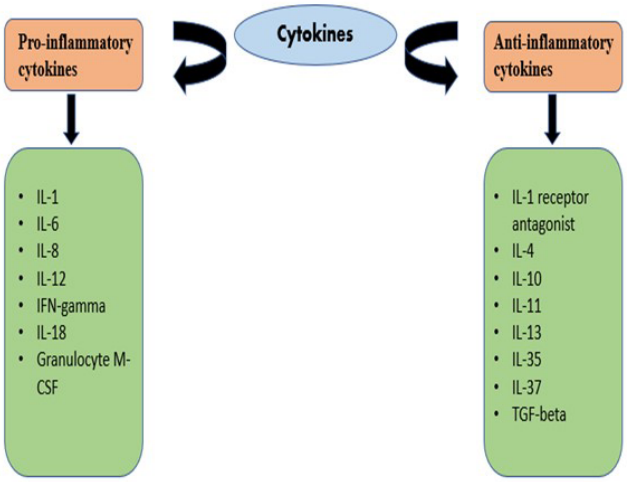


**Figure 5: Types of cytokines.**

Sometimes the same cytokine (such as IL-6) serves as both anti and pro-inflammatory cytokine (Borsini *et al*., 2020). This relies on the amount of cytokine, produced cytokine and the type of cell that is regulated, cytokine action sequences and even time period (Oliveira *et al*., 2011). When IL-4 is provided to triggered monocytes simultaneously it hinders the production of IL-6; In contrast, this increases the effect of IL-6 when it is added before any active signals (Chang *et al*., 2009; Oliveira *et al*., 2011). It is noted that the most significant anti-inflammatory cytokine is IL-10 during human immune response, produced by various immune cells (Houra *et al*., 2020). Anti-inflammatory cytokines performs a significant role in lowering the allergic reactions in skin and inflammation leading to reduction of Post-Inflammatory Hyperpigmentation (PIH).

After the adherence of pathogens specialize receptors, the stimulation of these receptors conciliate the formulation of inflammatory cytokines, IL-1, IL-6, TNF. These interleukin trigger the factors and antibodies to the site of inflammation (Snapper and Abraham, 2013). Inflammatory conciliators produced throughout inflammation, causes pain through sensation of nociceptors and direct activation of nociceptors (Atmaramani *et al*., 2020). The main issue with inflammation is not the means by which regularly it begins, but how frequently it fails to decline (Nathan and Ding, 2010). Physiological stress can also begin the inflammatory reaction, thus caused both mental and physical illness (Leonard, 2018).

*Proinflammatory cytokines*

*Interleukin-1 (IL-1)*

The first known interleukin, IL-1 (Schett *et al*., 2016), was discovered in 1979. It is an essential component for the regulation of innate and adaptive immune responses (Dinarello *et al*., 2012; Fields, 2019) and also involve in the regulation of inflammatory processes (Dinarello, 2009; Gallenga *et al*., 2019) by activating mediators (Capecchi *et al*., 2018). Both chronic and acute inflammations are

regulated by IL-1 (Dinarello *et al.*, 2012). Innate immunity is strongly regulated by IL-1 and the cytoplasmic domain of IL-1 receptor type I that binds IL-1, similar to the cytoplasmic domains of all (TLR's) toll like receptors. The consensus signals of IL-1 are further divided on the basis of secreted molecules into three subclasses. Subclass agnostic signals, (IL-1α, IL-18, IL-36α) triggers pro-inflammatory signals, subclass anti-inflammatory cytokine (IL-37) activate anti-inflammatory reactions (Schett *et al.*, 2016; Dinarello, 2018; Mantovani *et al.*, 2019) and subclass receptor antagonists (IL-1Rα and IL-36Rα) (Zhan *et al.*, 2020) inhibit inflammation (Netea *et al.*, 2015).

Mostly studied types of IL-1 are IL-1α, IL-1Rα and IL-1α. Agnostic forms that are involved in disorders of inflammation are IL-1α and IL-1β (Apte and Voronov, 2008). During cell necrosis and tissue damage, IL-1α is secreted (Rider *et al.*, 2011). It is an "Alarmin" cytokine (Mantovani *et al.*, 2019). IL-1 causes inflammation and connection in damaging tissues (Burzynski *et al.*, 2019). The defense cytokines that are produced in our body are IL-1β that specifically act against infections (Gallenga *et al.*, 2019). Dendritic cells (DC's), macrophages, and monocytes are often produced by IL-1β (Dinarello *et al.*, 2012) where B-lymphocytes and natural killer cells in less quantity are also produced by IL-1β (Dinarello, 2009, 2011). At tissue level powerful pro-inflammatory mediator is considered as IL-1β (Dinarello *et al.*, 2012). It causes vasodilation and induces the prostaglandins to expression phase and endorses the granulocytes to the site of inflammation such as inflamed tissue (Kim *et al.*, 2014) (Figure 6). IL-1Rα binds to the IL-1RI receptor and inhibits the IL-1α and IL-1β for performing its anti-inflammatory activity. IL-1 also induces its indirect effect on lymphocyte-mediated immunity; participate in pain, fever, hypotension, vasodilation, and all other diseases where there is direct inflammation (Conti *et al.*, 2018; Gallenga *et al.*, 2019).

*Interleukin-6 (IL-6)*

The group of IL (interleukin) - 6 comprises of seven cytokines involves IL-6, IL-11, LIF (leukemia inhibitory factor), OSM (oncostatin M), CT-1 (cardiotrophin-1), CLC (cardiotrophin-like cytokine), and CNTF (ciliary neurotrophic factor) (Jones and Jenkins, 2018). IL-27, IL-39, and IL-35, have recently been introduced into the family (Wang *et al.*, 2016b). IL-39 is a newly induced member from the IL-6 family, and comprises of EBI3 and IL-12p19 and transmits signals through the complex of gp130 and IL-23R, which is communicated by B cells and has pro-inflammatory capacities (Hasegawa *et al.*, 2016). IL-6 is known as pleiotropic cytokine (Kaur *et al.*, 2020) because it can treat both types of cytokines for example, pro and anti-inflammatory cytokine (Rose-Johnston, 2017; Zegeye *et al.*, 2020). Interleukin 6 (IL6) is a cytokine with numerous physiological activities that helps in metabolism regulation (Mauer *et al.*, 2015). The IL-6 signaling physiology is complex because the impacts of IL-6 on metabolism depend upon signal coordination between cell types (Schmidt-Arras and Rose-John, 2016) that include proinflammatory, noninflammatory and anti-inflammatory mechanisms. IL-6 cytokines containing 184 amino acids (Yang *et al.*, 2020).

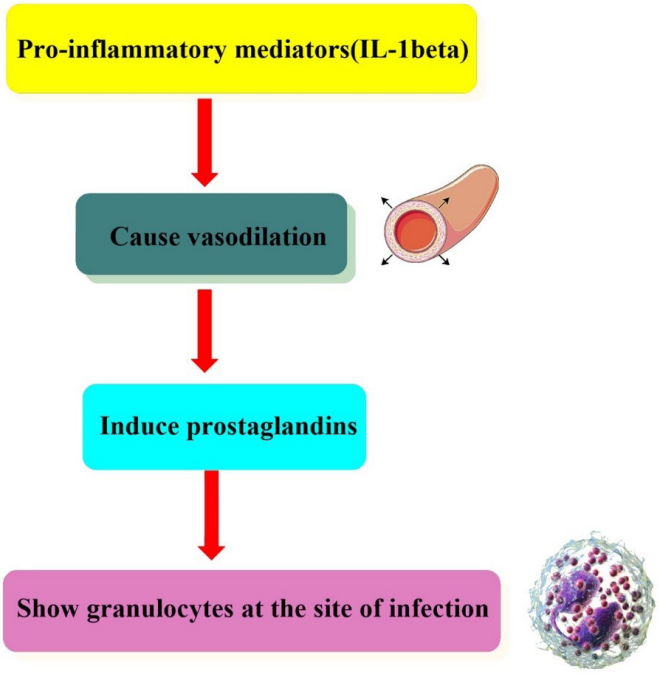


**Figure 6: Role of IL-1 in pro-inflammation.**

IL-6 is emitted by monocytes, macrophages, B-cells and T-cells (Wang *et al.*, 2020). The sub-atomic component of IL-6 signaling is intervened by IL-6 receptor α (IL6Rα) by the signaling protein IL6ST (also called as (glycoprotein-130) gp130) (Rose-Johnston, 2017). Accepted IL-6 signaling includes binding of IL-6 (Kang *et al.*, 2020) to an IL-6Rα with low affinity then IL-6/IL6Rα form complex with IL6ST (Reeh *et al.*, 2019) in the plasma membrane. Inhibitors focusing on IL-6 itself, JAK family proteins or IL-6Rα chain (IL6Rα) are effective against different insusceptible issues (Narazaki and Kishimoto, 2018). At the point when IL-6 bound to the IL-6R, this complex can tie to gp130, incorporating gp130 liable for their functional purposes (Schaper and Rise-John, 2015; Kang *et al.*, 2019; Zhang *et al.*, 2020). Consequently, it prompts intracellular signaling and initiates a pro-inflammatory response (Masjedi *et al.*, 2018).

It helps in B cell stimulation, metabolic regulation, and in keeping up balance between effectors and active T-cells. IL-6 initiates the Th17 cells and secretes IL-17 and IL-10 cytokines that generate Th17 cells to activate pathogenicity.In this way, IL-6 can discharge IL-1Rα and TNFα receptor that suppresses the function of IL-1 and TNFα respectively (Rose-Johnston, 2017) (Figure 7).

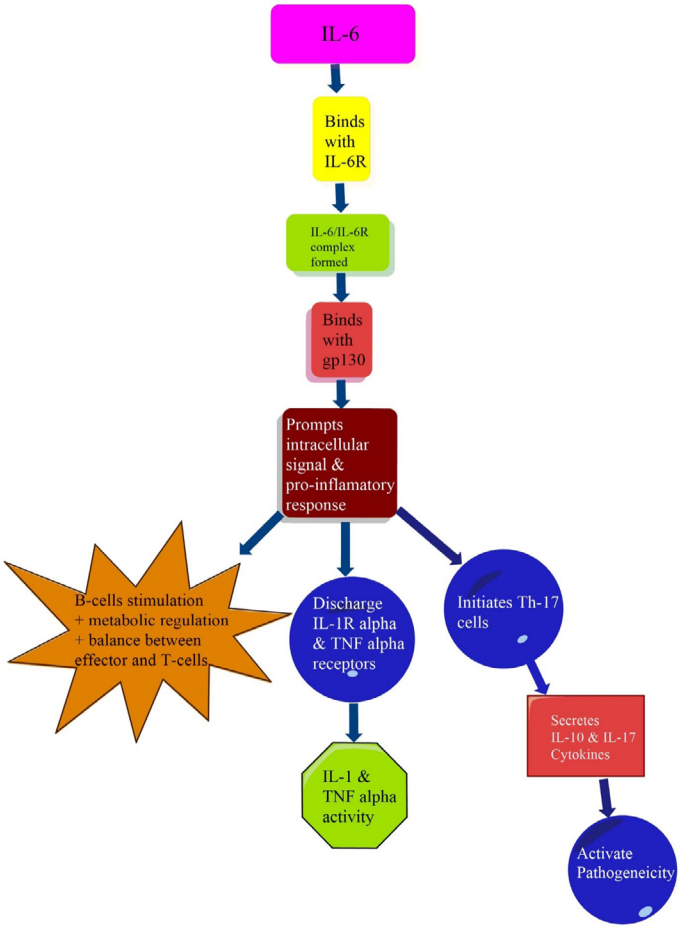


**Figure 7: Role of IL-6 in pro-inflammation.**

In inflammation, the function of IL-6 firmly fluctuates because of difference in stage and type of disease and it can be defensive or pathogenic (Fontes *et al.*, 2015). For pro-inflammatory reaction, IL-6 Trans signals in all gp130 communicating cells by the sIL-6R (Masjedi *et al.*, 2018). Though for anti-inflammatory reaction, IL-6 acts through its connection to the cell surface IL-6 receptor (Calabrese and Rose-John, 2014; Masjedi *et al.*, 2018).

*Anti-inflammatory cytokines*

*Interleukin-4 (IL-4)*

Interleukin-4 (IL-4) is a highly functional cytokine emitted by mast cells, basophils, T-helper 2 cells, eosinophils, stromal cells and epithelial cells (Gadani *et al.*, 2012; Pulendran and Artis, 2012; May and Fung, 2015; Paul, 2015). When IL-4 interacts with the IL-4 receptor, IL-4 signaling initiates a response that prompts to genes transcription of B and T cell activation (Goenka and Kaplan, 2011; Zeng *et al.*, 2014). IL-4 applies an anti-inflammatory activity by decreasing the activity and production of proinflammatory cytokines. It almost completely inhibits the production and synthesis of TNF-α and IL-1β. It suppresses the production of IL-6 and its activity when activated by endothelial cells (Shiau *et al.*, 2019). It also regulates the discharge of Th1 cytokines and restrains the production of chemokines that hire Th-1 cells in the area of infection (Gordon and Martinez, 2010; Lazarski *et al.*, 2013) (Figure 8).

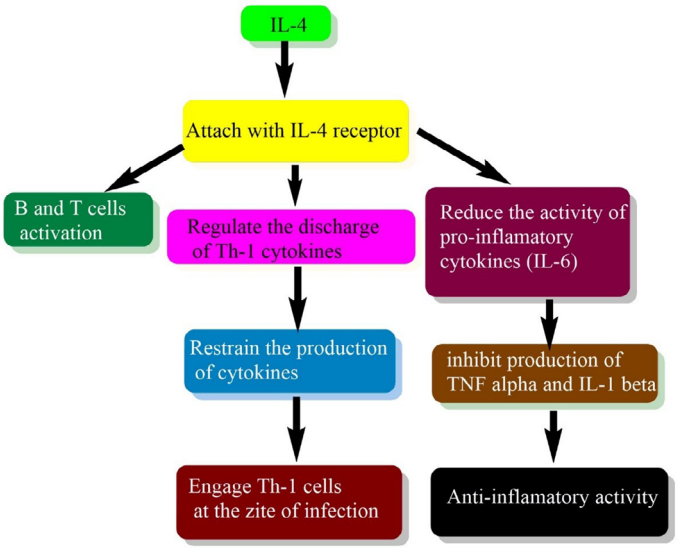


**Figure 8: Role of IL-4 in anti-inflammation.**

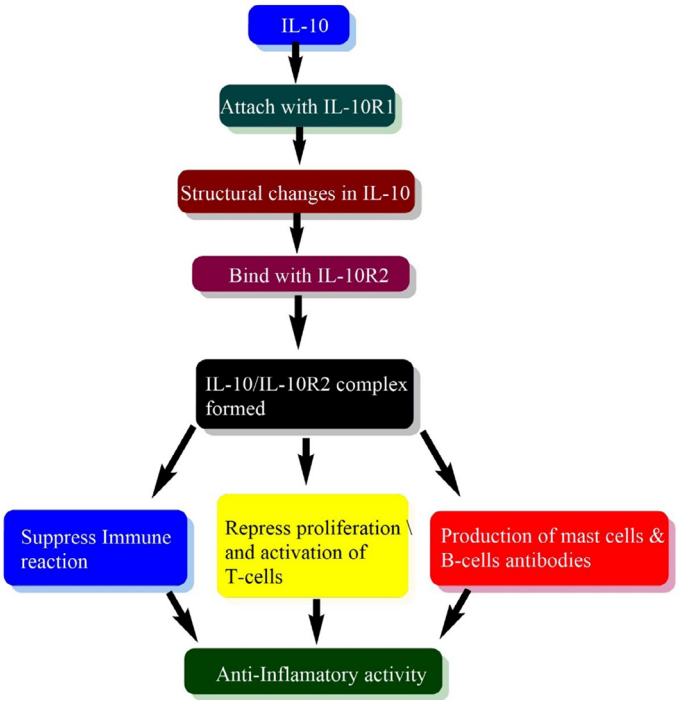


**Figure 9: Role of IL-10 in anti-inflammation.**

*Interleukin-10 (IL-10)*

IL-10 is considered to be a strong anti-inflammatory cytokine. Initially, it was called as cytokine amalgamation inhibitory factor (CSIF) as it can repress the production of IFN-c (proinflammatory cytokines) and TNFα (Ge *et al.*, 2020). Like many anti-inflammatory cytokines, IL-10 targets various (innate and adaptive) leukocytes to suppress their activity and function, while suppressing inflammatory cytokine bursts, preventing injury to the helper, and maintaining functional tissue integrity (Ng *et al.*, 2013). A wide range of cell types include dendritic cells (DC's), CD4 T cells, mast cells, macrophages, CD8 T cells, neutrophils, eosinophils, B cells, (cNKs) conventional natural killer cells and few (ILCs) innate lymphoid cells

have been reported to produce IL-10 (Fang and Zhu, 2020).

IL-10 attaches to IL-10R1 and then IL-10R2 (Yoon *et al.*, 2006, 2010). At the point, when IL-10 attaches to IL-10R1 it causes structural changes in IL-10 that causes its adhesion with IL-10R2 and IL-10/IL-10R complex. This complex suppresses the immune reactions (Dagvadorj *et al.*, 2008; Thibodeau *et al.*, 2008) and represses proliferation and activation of T cells (Saraiva *et al.*, 2020). It also promotes the multiplication and production of mast cells, thymocytes and B cells antibodies (Ragheb *et al.*, 2011) (Figure 9).

## Conclusions and Recommendations

The inflammation is related to most of the human diseases directly and indirectly. Currently there is no specific drug for inflammation and some of the general drugs that are being used have shown detrimental side effects. So it is a dire need of hour to find natural products which are effective against inflammation. It is recommended that natural products and medicinal plants should be used for the treatment of inflammation after its scientific evaluation and study because they do not have any adverse side effects which can damage systems and organs.

*Conflict of interest*

The authors have declared no conflict of interest.

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